

## WEST Search History

DATE: Thursday, June 08, 2006

<u>Hide?</u>	<u>Set Name</u>	<u>Query</u>	<u>Hit Count</u>
		<i>DB=PGPB,USPT; PLUR=YES; OP=OR</i>	
<input type="checkbox"/>	L10	restenosis and L9	74
<input type="checkbox"/>	L9	arthritis and L8	285
<input type="checkbox"/>	L8	asthma and L7	408
<input type="checkbox"/>	L7	11 or 12 or 13 or 14 or 15 or L6	3100
<input type="checkbox"/>	L6	549/59.ccls.	636
<input type="checkbox"/>	L5	548/318.5.ccls.	121
<input type="checkbox"/>	L4	546/290.ccls.	683
<input type="checkbox"/>	L3	514/444.ccls.	620
<input type="checkbox"/>	L2	514/389.ccls.	433
<input type="checkbox"/>	L1	514/345.ccls.	907

END OF SEARCH HISTORY

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAJRK1626

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 "Ask CAS" for self-help around the clock  
NEWS 3 DEC 23 New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/  
USPAT2  
NEWS 4 JAN 13 IPC 8 searching in IFIPAT, IFIUDB, and IFICDB  
NEWS 5 JAN 13 New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to  
INPADOC  
NEWS 6 JAN 17 Pre-1988 INPI data added to MARPAT  
NEWS 7 JAN 17 IPC 8 in the WPI family of databases including WPIFV  
NEWS 8 JAN 30 Saved answer limit increased  
NEWS 9 FEB 21 STN AnaVist, Version 1.1, lets you share your STN AnaVist  
visualization results  
NEWS 10 FEB 22 The IPC thesaurus added to additional patent databases on STN  
NEWS 11 FEB 22 Updates in EPFULL; IPC 8 enhancements added  
NEWS 12 FEB 27 New STN AnaVist pricing effective March 1, 2006  
NEWS 13 FEB 28 MEDLINE/LMEDLINE reload improves functionality  
NEWS 14 FEB 28 TOXCENTER reloaded with enhancements  
NEWS 15 FEB 28 REGISTRY/ZREGISTRY enhanced with more experimental spectral  
property data  
NEWS 16 MAR 01 INSPEC reloaded and enhanced  
NEWS 17 MAR 03 Updates in PATDPA; addition of IPC 8 data without attributes  
NEWS 18 MAR 08 X.25 communication option no longer available after June 2006  
NEWS 19 MAR 22 EMBASE is now updated on a daily basis  
NEWS 20 APR 03 New IPC 8 fields and IPC thesaurus added to PATDPAFULL  
NEWS 21 APR 03 Bibliographic data updates resume; new IPC 8 fields and IPC  
thesaurus added in PCTFULL  
NEWS 22 APR 04 STN AnaVist \$500 visualization usage credit offered  
NEWS 23 APR 12 LINSPEC, learning database for INSPEC, reloaded and enhanced  
NEWS 24 APR 12 Improved structure highlighting in FQHIT and QHIT display  
in MARPAT  
NEWS 25 APR 12 Derwent World Patents Index to be reloaded and enhanced during  
second quarter; strategies may be affected  
  
NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,  
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.  
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT  
<http://download.cas.org/express/v8.0-Discover/>  
  
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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 09:54:23 ON 19 APR 2006

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 09:54:32 ON 19 APR 2006

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STRUCTURE FILE UPDATES: 17 APR 2006 HIGHEST RN 880759-42-2

DICTIONARY FILE UPDATES: 17 APR 2006 HIGHEST RN 880759-42-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

\*\*\*\*\*  
\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

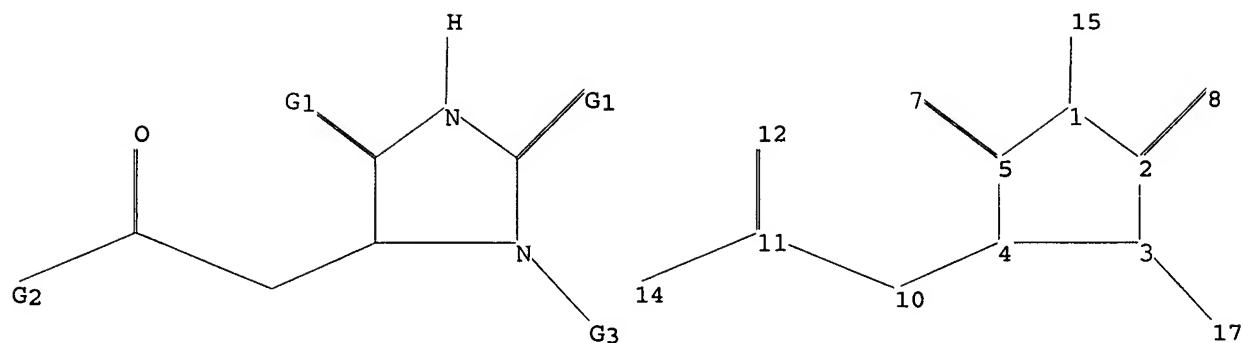
REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10525640\Struc 5.str

10525640ra.trn



chain nodes :

7 8 10 11 12 14 15 17

ring nodes :

1 2 3 4 5

chain bonds :

1-15 2-8 3-17 4-10 5-7 10-11 11-14 11-12

ring bonds :

1-2 1-5 2-3 3-4 4-5

exact/norm bonds :

1-2 1-5 2-3 2-8 3-4 3-17 4-5 5-7 11-14 11-12

exact bonds :

1-15 4-10 10-11

G1:O,S

G2:C,N

G3:H,CH3

Match level :

1:Atom 2:Atom 3:CLASS 4:Atom 5:Atom 7:CLASS 8:CLASS 10:CLASS 11:CLASS

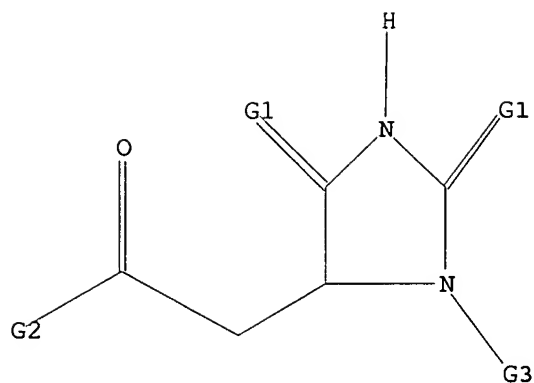
12:CLASS 14:CLASS 15:CLASS 17:CLASS

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS

L1 STR



G1 O,S

G2 C,N

G3 H,Me

Structure attributes must be viewed using STN Express query preparation.

=> l1

SAMPLE SEARCH INITIATED 09:54:47 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 50 TO ITERATE

100.0% PROCESSED 50 ITERATIONS

8 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 576 TO 1424

PROJECTED ANSWERS: 8 TO 329

L2 8 SEA SSS SAM L1

=> d scan

L2 8 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN L-Isoleucinamide, N-[6-[[6-[[[(2,5-dioxo-4-imidazolidinyl)acetyl]amino]-1-oxohexyl]amino]-1-oxohexyl]-L-isoleucyl-N-[1-(1H-indol-3-ylmethyl)-2,2-dimethoxyethyl]- (9CI)

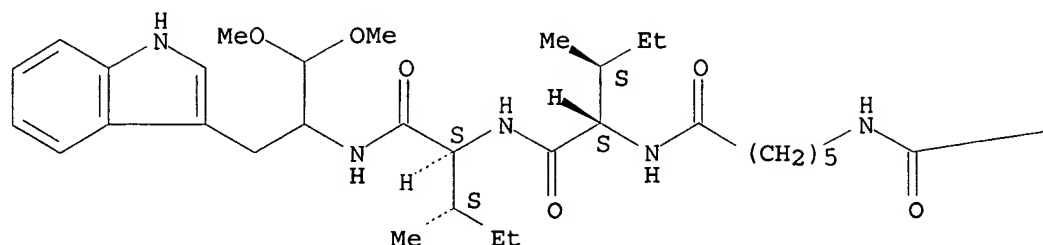
SQL 5

MF C42 H66 N8 O9

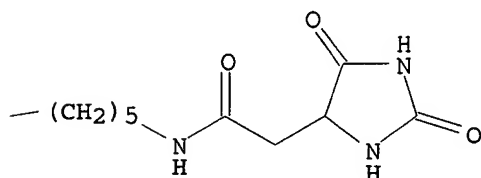
\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> l1 full

FULL SEARCH INITIATED 09:55:07 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 879 TO ITERATE

100.0% PROCESSED 879 ITERATIONS

241 ANSWERS

SEARCH TIME: 00.00.01

L3 241 SEA SSS FUL L1

=> file medline caplus

COST IN U.S. DOLLARS

SINCE FILE

ENTRY

TOTAL

SESSION

FULL ESTIMATED COST

166.94

167.15

FILE 'MEDLINE' ENTERED AT 09:55:12 ON 19 APR 2006

FILE 'CAPLUS' ENTERED AT 09:55:12 ON 19 APR 2006

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=> l3

L4 93 L3

=> dup rem l4

PROCESSING COMPLETED FOR L4

L5 93 DUP REM L4 (0 DUPLICATES REMOVED)

=> d ibib abs hitstr 81-93

10525640ra.trn

L5 ANSWER 81 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1956:64655 CAPLUS

DOCUMENT NUMBER: 50:64655

ORIGINAL REFERENCE NO.: 50:12084b-h

TITLE: Preparation of  $\beta$ -aminotricarballylic acid

AUTHOR(S): Dornow, Alfred; Rombusch, Konrad

CORPORATE SOURCE: Tech. Hochschule, Hannover, Germany

SOURCE: Chemische Berichte (1955), 88, 1334-40

CODEN: CHBEAM; ISSN: 0009-2940

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 50:64655

GI For diagram(s), see printed CA Issue.

AB  $\beta$ -Aminotricarballylic acid (I) was prepared by hydrolysis of esters of hydantoin-5,5-diacetic acid (II). A solution of 17.2 g. AcCHPrCO<sub>2</sub>Et, 40 g. (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub>, and 7.2 g. KCN in 170 ml. 55% EtOH heated 6 hrs. at 58-62°, 0.5 hr. at 80-90° (with alc. distillation), concd, in vacuo to 30 ml., and neutralized with HCl gave 9.9 g. NH<sub>4</sub>CO.NH<sub>4</sub>CO.CMeCHPrCO<sub>2</sub>Et (IIa), m. 86° (from H<sub>2</sub>O). CO(CH<sub>2</sub>CO<sub>2</sub>Et)<sub>2</sub> analogously gave 52% II Et ester (III), m. 143° (from 50% alc.), also prepared in 77% yield by refluxing  $\beta$ -ureidotricarballylic acid (IV) in absolute alc. saturated with HCl 3 hrs. II Me ester, prepared

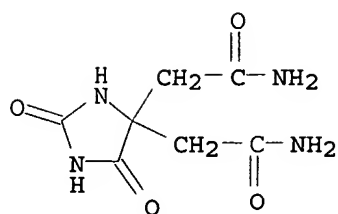
similarly in

47% yield from CO(CH<sub>2</sub>CO<sub>2</sub>Me)<sub>2</sub>, m. 156° (from 50% MeOH); esterification of II with absolute MeOH and dry HCl gave 86% of a 2nd modification (V), m. 210° (from 50% MeOH). V was also prepared in 74% yield from IV and MeOH-HCl, or in 53% yield from 0.95 g. I and 0.51 g. KCNO refluxed 0.5 hr. in H<sub>2</sub>O and the IV esterified. The infrared spectra of these modifications are given and compared. Other esters of II prepared from the corresponding CO(CH<sub>2</sub>CO<sub>2</sub>R)<sub>2</sub> (VII) were (R, m.p., and % yield): iso-Pr, 200-1° (from 50% EtOH), 48%; Bu, oil, 27%; and sec-Bu, 131-2° (from 50% EtOH), 54%. VII prepared by saturating CO(CH<sub>2</sub>CO<sub>2</sub>H)<sub>2</sub> in ROH with anhydrous HCl were (R, b.p., % yield): iso-Pr, b1.0 101-2.5°, 42%; Bu, b1.0 138-9° 43%; and sec-Bu, b0.9 117-18°, 45%. Hydantoin-5,5-dipropionic acid, prepared like IIa in 49% yield from CO(CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H)<sub>2</sub> (VIII), m. 171° (from 50% EtOH). II, m. 190-2°, was prepared in 40% yield by refluxing 13.6 g. III 3 hrs. with 100 ml. 20% HCl, or in 74% yield by letting 1.36 g. III stand 7 days in 500 ml. saturated Ba(OH)<sub>2</sub>. CO(CH<sub>2</sub>CO<sub>2</sub>H)<sub>2</sub> (14.6 g.), treated like VIII gave 13° II and 4.8 g. 5,5-dimethylhydantoin. II diamide (0.27 g.) from 0.5 g. III and 30 ml. 40% aqueous NH<sub>3</sub> 5 days at room temperature, m. 248° (decomposition) (from H<sub>2</sub>O); II dihydrazide (9.6 g.), from 1.35 g. III and 1.0 g. (NH<sub>2</sub>)<sub>2</sub>.-H<sub>2</sub>O refluxed 3 hrs. in alc., m. 153-4° (from 50% EtOH). III (2.72 g.) refluxed in a saturated solution of 7.8 g. Ba(OH)<sub>2</sub> 8H<sub>2</sub>O until turbidity and NH<sub>3</sub> evolution occur (1.5 hrs.), the Ba<sup>++</sup> precipitated with H<sub>2</sub>SO<sub>4</sub>, and the solution evaporated in vacuo gave 1.6 g. IV, m. 267° (decomposition) (from H<sub>2</sub>O). Esters of II (0.01 mole) heated 4-9 hrs. at 150-200° with 11.0 g. Ba(OH)<sub>2</sub> 8H<sub>2</sub>O or 2 g. NaOH and 50 ml. H<sub>2</sub>O gave 54-78% I, m. 227-9° (decomposition) or 200° (rapid heating) (from 80% EtOH). II Me ester and Ba(OH)<sub>2</sub> 6 hrs. at 180° gave 78% I; ° I Me ester.HCl, m. 155-7°; I Et ester.HCl, m. 162-4° I forms blue, voluminous, insol. Cu<sub>1</sub>.5C<sub>6</sub>H<sub>6</sub>O<sub>6</sub>N with aqueous Cu(OAc)<sub>2</sub>. The median sedative dose of II for mice is 380 mg./kg. (oral); the lethal dose, 2000 mg./kg.

IT 858222-48-7, 4,4-Imidazolidinediacetamide, 2,5-dioxo-  
(preparation of)

RN 858222-48-7 CAPLUS

CN 4,4-Imidazolidinediacetamide, 2,5-dioxo- (5CI) (CA INDEX NAME)



L5 ANSWER 82 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1953:54770 CAPLUS

DOCUMENT NUMBER: 47:54770

ORIGINAL REFERENCE NO.: 47:9273c-i

TITLE: Thiohydantoins. I. Preparation of some 2-thiohydantoins from amino acids and acylamino acids

AUTHOR(S): Swan, J. M.

CORPORATE SOURCE: Commonwealth Sci. Ind. Research Organization, Melbourne

SOURCE: Australian J. Sci. Res. (1952), A5, 711-20

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

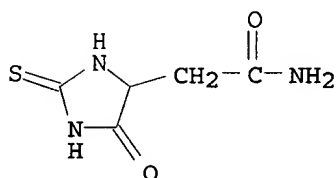
AB Valine (I), methionine (II), isoleucine (III), PhCH(NH<sub>2</sub>)CO<sub>2</sub>H (IV), tryptophan (V), histidine (VI), and tyrosine (VII), or their Ac derivs. have been converted by warming with Ac<sub>2</sub>O and NH<sub>4</sub>SCN (VIII) into the corresponding 1-acetyl-2-thiohydantoins (IX), which were deacetylated by an improved procedure. Warming 1.2 g. I and 0.9 g. VIII in 10 ml. Ac<sub>2</sub>O containing 10% AcOH, and evaporating the solution, give the corresponding IX derivative,

C<sub>8</sub>H<sub>12</sub>O<sub>2</sub>N<sub>2</sub>S, m. 112° (from EtOH). The same method furnishes C<sub>11</sub>H<sub>10</sub>O<sub>2</sub>N<sub>2</sub>S, m. 199-201°, from IV; C<sub>9</sub>H<sub>14</sub>O<sub>2</sub>N<sub>2</sub>S, m. 162-3°, from III; C<sub>8</sub>H<sub>12</sub>O<sub>2</sub>N<sub>2</sub>S<sub>2</sub>, m. 102-3°, from II; and C<sub>14</sub>H<sub>13</sub>O<sub>2</sub>N<sub>3</sub>S, m. 172°, from V. Partial hydrolysis of AcNHCH(CO<sub>2</sub>Et)<sub>2</sub> with alc. KOH gives Et H acetamidomalonate (X), m. 140-1.5°. Warming X with Ac<sub>2</sub>O, AcOH, and VIII yields Et 1-acetyl-2-thio-5-hydantoincarboxylate, m. 108-9° (from CHCl<sub>3</sub>-petr. ether). X let stand with concentrated NH<sub>3</sub> gives AcNHCH<sub>2</sub>CONH<sub>2</sub>, m. 137-7.5°, and 1-acetyl-2-thiohydantoin (XI), m. 179°. PhCH<sub>2</sub>CONHCH(CO<sub>2</sub>H)CO<sub>2</sub>Et with VIII, Ac<sub>2</sub>O, and AcOH on a steam bath, gives Et 1-phenylacetyl-2-thio-5-hydantoincarboxylate, m. 110°. PhCH<sub>2</sub>CONHCH(CO<sub>2</sub>Et)<sub>2</sub> with KOH in EtOH at room temperature gives in 12 hrs. the free acid, C<sub>11</sub>H<sub>11</sub>O<sub>5</sub>N, m. 142° (127° by rapid heating). 1-Acetyl-5-(1-acetyl-4-imidazolylmethyl)-2-thiohydantoin, (XII), 187-8°, seps. when VIII, Ac<sub>2</sub>O, and AcOH are shaken with monoacetylhistidine hydrate or with anhydrous NaOAc and DL-histidine-HCl.2H<sub>2</sub>O. Hydrolyzing XII by cold EtOH, by refluxing 3 hrs. with N AcOH or by letting stand 3 hrs. in N NaOH gives 5-(1-acetyl-4-imidazolylmethyl)-2-thiohydantoin, m. 228-9°. Shaking with VIII, Ac<sub>2</sub>O, and AcOH converts N,N'-diacetylcystine into 5,5'-(dithiodimethylene)bis(1-acetyl-2-thiohydantoin), m. 198-202°, and N,N'-diacetyllysine into 5-(4-acetamidobutyl)-2-thiohydantoin, m. 194°. Heating VII with Ac<sub>2</sub>O, AcOH, and VIII produces 2 isomeric acetylthiohydantoins, (probably O- and N-Ac), m. 144°, λ<sub>maximum</sub> 279 mμ, ε 18,300, λ<sub>min.</sub> 249 mμ, ε 6000, and m. 208-9°, λ<sub>maximum</sub> 279 mμ, ε 15,800, λ<sub>min.</sub> 249 mμ, ε 3750. IX are hydrolyzed by refluxing with water or N AcOH, or by heating to 70° with 2N NH<sub>3</sub>, but not with HgCl<sub>2</sub> in EtOH to give the following RCH.CO.NH.CS.NH (XIIA) (R and m.p. given): H, 227° (decomposition): Me, 227° (decomposition); iso-Pr, 159-60°; iso-Bu, 172-3°;



MeSCH<sub>2</sub>CH<sub>2</sub>, 148-9°; Ph, 223-5°; 3-indolyl, 190-1°;  
H<sub>2</sub>NCOCH<sub>2</sub>, 246°; H<sub>2</sub>NCOCH<sub>2</sub>CH<sub>2</sub>, 190-1°; EtO<sub>2</sub>C, 227°.  
N-Acetylthreonine in the cold with Ac<sub>2</sub>O, AcOH, and VIII gives  
5-ethylidene-2-thiohydantoin (XIII), m. 263-4°, also synthesized by  
heating anhydrous Pb(OAc)<sub>2</sub>, 1-acetyl or 1-benzoyl-2-thiohydantoin, or XI and  
AcH in a sealed tube 3 hrs. at 90°, or by heating  
2-phenyl-4-ethylidene-5(4H)oxazolone, Ac<sub>2</sub>O, and VIII in a sealed tube 6  
hrs. at 105°. 5-Benzylidene-2-thiohydantoin, 258°, seps.  
when 2-methyl-, or 2-phenyl-4-benzylidene-5(4H)-oxazolone is heated with  
VIII and AcOH in a sealed tube 4-24 hrs. at 105°.

IT 64419-95-0, 5-Hydantoinacetamide, 2-thio-  
(preparation of)  
RN 64419-95-0 CAPLUS  
CN 4-Imidazolidineacetamide, 5-oxo-2-thioxo- (9CI) (CA INDEX NAME)



L5 ANSWER 83 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1954:18107 CAPLUS  
DOCUMENT NUMBER: 48:18107  
ORIGINAL REFERENCE NO.: 48:3266g-i,3267a-c  
TITLE: 5-Phenylhydantoin  
AUTHOR(S): Klosa, Josef  
SOURCE: Arch. Pharm. (1952), 285, 274-80  
DOCUMENT TYPE: Journal  
LANGUAGE: Unavailable  
OTHER SOURCE(S): CASREACT 48:18107

AB 5-Phenylhydantoin (I) and several derivs. have been prepared. I, m.  
181-3° (from EtOH), was prepared in 67-g. yield by triturating 100 g.  
of the BzH-NaHSO<sub>3</sub> addition compound with 223 g. (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> and 56 g. KCN,  
pouring 500 ml. 60% EtOH over the mixture, heating 5 hrs. at 50° and  
1 hr. at 70-90°, cooling, filtering off the inorg. salts, distilling  
off the EtOH, diluting the aqueous residue with double its volume of H<sub>2</sub>O,  
adjusting  
the pH of the solution to 2-3 with 2N HCl, refluxing 1 hr., filtering hot,  
and cooling. 2-Ureido-2-phenylacetic acid, m. 161-3° (from H<sub>2</sub>O),  
was prepared by warming 10 g. I in 50 ml. N aqueous NaOH 30 min. on the water  
bath, filtering, cooling, acidifying with concentrated HCl, and letting stand

24 hrs. 2-Amino-2-phenylacetic acid, crystalline powder, m. 252°, was  
prepared in 0.8-g. yield by refluxing 2 g. I in 10 ml. 33% NaOH 2 hrs.,  
diluting with 10 vols. H<sub>2</sub>O, cooling, and acidifying with concentrated HCl.  
Bi(phenylhydantyl) (C<sub>18</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>), crystalline powder, m. 343-5°, was  
prepared in 1.2-g. yield by refluxing 2 g. I with a solution of 2 g. Na in 50  
ml. EtOH 1 hr., cooling, diluting with 10 vols. H<sub>2</sub>O, filtering, and  
acidifying. 3-Methyl-5-phenylhydantoin, m. 161-3° (from H<sub>2</sub>O), was  
prepared in 5.5 g. yield by adding 30 g. Me<sub>2</sub>SO<sub>4</sub> with cooling to 10 g. I in  
100 ml. 2N NaOH, and warming 20 min. to 60°. 1,3-Dimethyl-5-  
phenylhydantoin, m. 107-8° (from H<sub>2</sub>O), was prepared in 4.4-g. yield  
by treating 5 g. I in 50 ml. 2N NaOH with 25 ml. Me<sub>2</sub>SO<sub>4</sub> (the pH must be  
7-10 during addition), and cooling. 5-Phenyl-5-bromohydantoin (II), m.

210-12°, was prepared in 49 g. yield by adding 75 g. Br in 145 ml. glacial AcOH to 60 g. I in 250 ml. glacial AcOH, heating 4 hrs. on the steam bath, and letting stand. 5-Phenyl-5-piperidinohydantoin, m. 220-2°, was prepared in 8.3-g. yield by adding 12 ml. piperidine to a suspension of 10 g. II in 150 ml. absolute Et<sub>2</sub>O, refluxing 1 hr., and

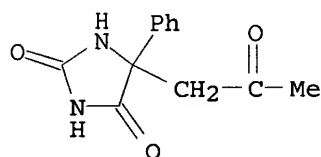
evaporating

to half the original volume 5-Phenyl-5-acetonylhydantoin, m. 206-8° (from EtOH), was prepared in 2.6-g. yield by carefully warming 3 g. II with 30 ml. Me<sub>2</sub>CO to start the exothermic reaction, letting the reaction proceed without further warming finally heating 30 min. at 40°, cooling, and diluting with 3 vols. H<sub>2</sub>O.

IT 858204-23-6, Hydantoin, 5-acetonyl-5-phenyl-  
(preparation of)

RN 858204-23-6 CAPLUS

CN Hydantoin, 5-acetonyl-5-phenyl- (5CI) (CA INDEX NAME)



L5 ANSWER 84 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1949:17411 CAPLUS

DOCUMENT NUMBER: 43:17411

ORIGINAL REFERENCE NO.: 43:3362g-i,3363a-i,3364a-d

TITLE: Biosynthesis of penicillins. VI. N-2-Hydroxyethyl amides of some polycyclic and heterocyclic acetic acids as precursors

AUTHOR(S): Jones, Reuben G.; Soper, Quentin F.; Behrens, Otto K.; Corse, Joseph W.

SOURCE: Journal of the American Chemical Society (1948), 70, 2843-8

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 43:17411

AB 2,6-MeCl<sub>10</sub>H<sub>6</sub>NH<sub>2</sub> (78 g.) in 80 mL. concentrated HCl and 200 mL. H<sub>2</sub>O at 0°, treated at 5° with 35 g. NaNO<sub>2</sub> in 50 mL. H<sub>2</sub>O and, after 0.5 h., with 130 g. ice-cold 42% HBF<sub>4</sub>, gives 90% of the 2-diazonium fluoroborate, decomposition of which yields 69% 2-methyl-6-fluoronaphthalene (I), m. 77°. I (40 g.) at 210°, treated (15 min.) with 40 g. Br (with illumination with a 100-w. lamp), gives 82% 2-(bromomethyl)-6-fluoronaphthalene (II), b<sub>2</sub> 125-30°, m. 53°. II (48 g.), added to a refluxing solution of 30 g. KCN in 60 mL. H<sub>2</sub>O and 200 mL. EtOH, the EtOH removed after refluxing 4 h., 500 mL. H<sub>2</sub>O added, the solution extracted

with ether, and the residue from the ether boiled 5 h. with 40 g. KOH in 40 mL. H<sub>2</sub>O and 200 mL. EtOH, gives 74% 6-fluoro-2-naphthaleneacetic acid, m. 138-9° (Me ester, b<sub>2</sub> 163-6°, m. 48-9°).

2,6-MeCl<sub>10</sub>H<sub>6</sub>NH<sub>2</sub> (63 g.) in 100 mL. H<sub>2</sub>O and 700 g. 48% HBr, treated (3-4 h.) at 5° with 45 g. NaNO<sub>2</sub> in 75 mL. H<sub>2</sub>O and the diazonium solution poured (10 min.) into 170 g. CuBr in 800 mL. 48% HBr at 70-80°, gives 40% 6-bromo-2-methylnaphthalene (III), m. 142° III yields 80% 6-bromo-2-(bromomethyl)naphthalene, m. 124-5° this gives 69% 6-bromo-2-naphthaleneacetic acid, m. 175-6° (Me ester, b<sub>2</sub>

187-93°, m. 67-9°). 3,2-ClC<sub>10</sub>H<sub>6</sub>CHO (32.5 g.), 35 g. hippuric acid, 14.5 g. anhydrous AcONa, and 50 mL. Ac<sub>2</sub>O, heated on the steam bath 1 h., give 75% 2-phenyl-4-(3-chloro-2-naphthylmethylene)-5(4H)-oxazolone (IV), bright yellow, m. 192° 40 g. IV in 200 mL. 10% NaOH, refluxed 9 h., the mixture diluted to 1500 mL. with H<sub>2</sub>O, washed with ether, the aqueous solution treated with 20 mL. 12.5 N NaOH and 15 mL. 30%

H<sub>2</sub>O<sub>2</sub>,

allowed to stand overnight, the filtrate acidified with HCl, extracted with ether-C<sub>6</sub>H<sub>6</sub>, and the residue esterified, gives 37% Me 3-chloro-2-naphthaleneacetate, b<sub>2</sub> 163-5°, m. 49-50° the free acid m.

193-4°. 6,2-MeOC<sub>10</sub>H<sub>6</sub>Ac (100 g.), 25.5 g. S, and 87 g. morpholine, heated 18 h. at 140°, part of the morpholine removed in vacuo, 250 mL. AcOH and 350 mL. concentrated HCl added, and the mixture refluxed 24 h.,

give

67% 6-methoxy-2-naphthaleneacetic acid, m. 203-5° (Me ester, b<sub>1</sub> 192-3°, m. 86°, 73%). 5,6,7,8-Tetrahydro-2-acetonaphthone (50 g.), 13 g. S, and 40 mL. morpholine, refluxed overnight, 400 mL. concentrated HCl and 300 mL. H<sub>2</sub>O added, and the mixture again refluxed

overnight,

followed by esterification with EtOH and H<sub>2</sub>SO<sub>4</sub>, give Et

5,6,7,8-tetrahydro-2-naphthaleneacetate, b<sub>0.5</sub> 140-3°.

2-Acetylphenanthrene (13.2 g.), 3.2 g. S, and 10.5 g. morpholine, heated 15 h. at 160°, the mixture treated with 150 mL. AcOH and 36% HCl, and refluxed 24 h., give 81% 2-phenanthreneacetic acid, m. 187-8° the 3-isomer m. 174-5°, 84% (Me ester, b<sub>1.5</sub> 203-5°, 89%).

8-(Bromomethyl)quinoline (120 g.) in 250 mL. warm EtOH, added (0.5 h.) to 50 g. KCN in 100 mL. warm H<sub>2</sub>O and the mixture refluxed 1.5 h., gives 78% 8-(cyanomethyl)quinoline, m. 86-7°; hydrolysis with aqueous alc. KOH and esterification give 91% Et 8-quinolineacetate, b<sub>3</sub> 158-60°. Et 3-quinolinecarboxylate (70 g.), 62 g. AcOEt, and EtONa (12 g. Na and 0.52 mol absolute EtOH) in 100 cc. dry C<sub>6</sub>H<sub>6</sub>, refluxed 20 h., the cooled solution poured onto ice, diluted to 5 l. with H<sub>2</sub>O, treated with 50 mL. 12 N NaOH, washed with two 300 mL. portions of ether, and the aqueous solution neutralized with dilute H<sub>2</sub>SO<sub>4</sub> and extracted with two 500-mL. portions of ether, give 75% Et 3-quinolylformylacetate, m. 84° 27 g. of the keto ester in 125 g. 25% H<sub>2</sub>SO<sub>4</sub>, heated 30 min. at 100°, gives 95% 3-acetylquinoline (V).

V (7 g.), 5 g. S, 50 mL. (NH<sub>4</sub>)<sub>2</sub>S, and 25 mL. H<sub>2</sub>O, heated 20 h. at 145-50°, the residue extracted with two 300-mL. portions boiling 5% HCl, the solution refluxed 3 h., and the crude acid esterified, give 19% Et 3-quinolineacetate, b<sub>2.5</sub> 140-2°. pH<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CO<sub>2</sub>H (46 g.), 10.5 g. FeSO<sub>4</sub>, 115 g. C<sub>3</sub>H<sub>5</sub>(OH)<sub>3</sub>, 23 g. PhNO<sub>2</sub>, and 53 mL. concentrated H<sub>2</sub>SO<sub>4</sub>, boiled 5 h., give 37 g. crude acid which, esterified with EtOH and HCl, gives 39% Et 6-quinolineacetate, b<sub>3</sub> 160° the free acid (VI) m.

218-20°. Et 6-quinolinecarboxylate and AcOEt, condensed with EtONa, give 87% Et 6-quinolineacetate, hydrolysis of which with 25% H<sub>2</sub>SO<sub>4</sub> at 100° gives 90% 6-acetylquinoline, m. 76° the Willgerodt reaction gives 87.5% VI. 3,4 O<sub>2</sub>N(H<sub>2</sub>N)C<sub>6</sub>H<sub>3</sub>CO<sub>2</sub>H (108 g.) in 350 mL. concentrated HCl, treated with 125 g. Sn in portions (temperature below 90°), gives 87% (3,4-diaminophenyl)acetic acid-2HCl (VII), m. 222-4°

(decomposition); Et ester-2HCl (VIII), m. 185-7° (decomposition); 3 g. VII and 20 mL. 98-100% HCO<sub>2</sub>H, heated several hrs., give 100% 5-benzimidazoleacetic acid-HCl, m. 240-2° the Et ester m.

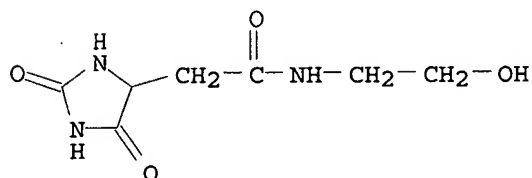
65-6°, 75%. VIII (14 g.) in 200 mL. ice H<sub>2</sub>O, treated with excess COCl<sub>2</sub>, gives 95% Et 2-hydroxy-5-benzimidazoleacetate, m. 208-9°.

NCCH<sub>2</sub>CO<sub>2</sub>Et (113 g.) and 15 g. (HOCH<sub>2</sub>CH<sub>2</sub>)<sub>3</sub>N in 100 mL. absolute EtOH, treated with a slow stream of H<sub>2</sub>S, the mixture poured after 5 days into ice-H<sub>2</sub>O, and 38 g. of the resulting oil and 23.1 g. ClCH<sub>2</sub>Ac in 300 cc. anhydrous ether kept 4 days, give 20.6 g. Et 4-methyl-2-thiazoleacetate, b<sub>17</sub>

136-9°. Thiaxanthrol (42 g.), 30 g. CH<sub>2</sub>(CO<sub>2</sub>H)<sub>2</sub>, and 80 mL. C<sub>5</sub>H<sub>5</sub>N, heated 2 h. at 60-70° and 2 h. at 90-5° and the liquid

poured into 600 mL. 2 N HCl, give 90% 9-thiaxantheneacetic acid, m. 167-8° (Me ester, b2 182-4°). The Ag salt of 2-benzylimidazole (53 g.) and 50 g. BrCH<sub>2</sub>CO<sub>2</sub>Et in 200 mL. xylene, refluxed 48 h., give 25.4% of the Et ester, m. 70-70.5°, of 2-benzyl-1-imidazoleacetic acid, m. 173-4°. Me 1-acenaphtheneacetate, b4 176-8°. N-2-Thienylacetyl-DL-valine m. 110-12°. Amides were prepared by heating the Me or Et ester of the various acids with a slight excess of HOCH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> at 100-150° for several hrs.; R in RCH<sub>2</sub>CONHCH<sub>2</sub>CH<sub>2</sub>OH is given, together with S (see part V). 2-Cl<sub>10</sub>H<sub>7</sub> m. 125-7°, S 1.3; 1-bromo-2-naphthalene m. 155-6°, S 0.5; 6-fluoro-2-naphthalene m. 145-6°, S 1.2; 3-chloro-2-naphthalene m. 150-1°, S 0.3; 6-bromo-2-naphthalene m. 167-8°, S 0.9; 5,6,7,8-tetrahydro-2-naphthalene m. 88-90°, S 0.9; 1-nitro-2-naphthalene m. 154-5°, S 0.9; 6-methoxy-2-naphthalene m. 160°, S 1.1; 1-acenaphthene m. 160°, S 1.1; 9-fluorene m. 127-8°, S 0.7; 2-phenanthrene m. 135-7°, S 0.5; 3-isomer m. 133-5°, S 0.5; 1-pyrrole m. 85-7°, S 0.9; 2-thiophene m. 66-7°, S 1.8; 2-furan oil, S 0.4; 2,6-dihydroxy-5-pyrimidine m. 271-2°, S 1; 2-methyl-4-hydroxy-5-pyrimidine m. 184°, S 0.9; 3,4-methylenedioxyphenyl m. 99-100°, S 1; 2-methyl-4-thiazole m. 93-4°, S 0.85; 4-methyl-2-thiazole m. 80-2°, S 0.9; 2-pyridine m. 93-4°, S 1; 3-isomer m. 94° S 1; 6-methyl-2-pyridine m. 49-50°, S 1; 2-benzyl-1-imidazole m. 177-9°, S 1; 3-quinoline m. 151-2°, S 1; 6-isomer m. 135°, S 1; 8-isomer m. 92-3°, S 1; 2-benzimidazole m. 185-90°, S 1; 5-isomer m. 160-2°, S 1; 2-hydroxy-5-benzimidazole m. 245-6°, S 1; 7-hydroxy-4-coumarin m. 114-16°, S 1; 9-xanthene m. 157-8°, S 0.8; 9-thiaxanthene m. 148-9°, S 0.7; 5-hydantoin m. 160-2°, S 0.9. Only a few of these compds. appeared to be utilized readily by the mold for the formation of new penicillins. Several of the compds. appeared to effect some increase in penicillin yield or to change the differential assay value of the crude penicillin produced in their presence.

IT 858208-01-2, 5-Hydantoinacetamide, N-2-hydroxyethyl-  
(preparation of)  
RN 858208-01-2 CAPLUS  
CN 5-Hydantoinacetamide, N-2-hydroxyethyl- (5CI) (CA INDEX NAME)



L5 ANSWER 85 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1944:39000 CAPLUS  
DOCUMENT NUMBER: 38:39000  
ORIGINAL REFERENCE NO.: 38:5800b-f  
TITLE: Synthesis of 5-(substituted-methyl)-5-phenethylhydantoins  
AUTHOR(S): Hénze, Henry R.; Holder, Charles B.  
SOURCE: Journal of the American Chemical Society (1944), 66, 1545-7  
CODEN: JACSAT; ISSN: 0002-7863  
DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C. A. 35, 5891.1. 1-Chloro-4-phenyl-2-butanone (40 g.), 31.4 g. KCN, 69.4 g. (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> and 500 cc. 65% EtOH, heated at 58-60° for 20 h., most of the alc. evaporated (separation of 18.1 g. of a dark red viscous oil)

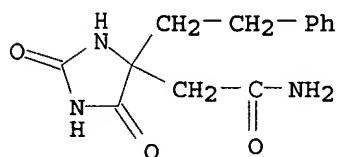
and

the solution acidified, give 26% of 5-phenethyl-5-hydantoinacetonitrile (I), m. 188-9° (corrected); petr. ether extraction of the oil yields a compound (II) (C<sub>21</sub>H<sub>20</sub>N<sub>2</sub>(?)), m. 96° (corrected). If the above reaction is carried out with 15.7 g. KCN, there results very little I, a somewhat larger yield of II and 22 g. of a solid whose m. p. increased from 160° to 230° on successive crystns.; it is not soluble in 20% NaOH. Hydrolysis of I with EtOH-HCl gives 47-70% of Et 5-phenethyl-5-hydantoinacetate (III), m. 156.7-7.7° (corrected). Details are given of the reaction of PhCH<sub>2</sub>CH<sub>2</sub>COCl and AcCHNaCO<sub>2</sub>Et and the isolation of a crude Et hydrocinnamoylacetate (IV), b<sub>4</sub> 127-34°, n<sub>20</sub>D 1.5058, d<sub>20</sub> 1.0679; with KCN and (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> in 55% EtOH IV gives 55% of crude III. III and concentrated NH<sub>4</sub>OH, allowed to stand 2 wk, give 52% of 5-phenethyl-5-hydantoin-acetamide (V), m. 228.7-9.7° (corrected). Solution of III in a slight excess of 10% NaOH and acidification of the cooled solution with 6 N HCl give 48% of 5-phenethyl-5-hydantoin-acetic acid (VI), m. 213-14.5° (corrected); VI results in 44% yield by refluxing I with 25% HCl for 20 h. or from V with 6 N HCl. II is apparently formed from interaction of 2 mols. of the ketone with KCN and (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> but not from the action of either alone; II must be heterocyclic, possess aromatic properties and but 1 active H atom; II is quite resistant toward hydrolysis, oxidation and reduction; alc. HCl (heated 20 h. on a steam cone) gives a compound C<sub>21</sub>H<sub>22</sub>N<sub>2</sub>O, m. 153.2-4.2° (corrected). A preliminary report is given of the pharmacol. properties of 5-diethylamino-, 5-dipropylamino- and 5-(4-morpholinyl)-5-phenethylhydantoins.

IT 858786-59-1, 5-Hydantoinacetamide, 5-phenethyl-  
(preparation of)

RN 858786-59-1 CAPLUS

CN 5-Hydantoinacetamide, 5-phenethyl- (4CI) (CA INDEX NAME)



L5 ANSWER 86 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1941:42326 CAPLUS

DOCUMENT NUMBER: 35:42326

ORIGINAL REFERENCE NO.: 35:6577b-e

TITLE: Preparation of certain 5-acetates and 5-acetamides of 5-phenylhydantoin

AUTHOR(S): Rogers, Burl G.; Henze, Henry R.

SOURCE: Journal of the American Chemical Society (1941), 63, 2190-1

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB Heating a mixture of 19.2 g. of BzCH<sub>2</sub>CO<sub>2</sub>Et, 13 g. KCN and 45.5 g. (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> in 350 cc. 60% EtOH for 10 hrs. at 58-62° gives 60% of the Et ester, m. 139-40° (all m. ps. corrected), of 5-phenyl-5-hydantoinacetic acid (I), m. 261.5-2.5° (decomposition) (prepared in 87% yield from the

ester by boiling 20 g. with 50 cc. 20% HCl for 3 hrs.). Esters of I were prepared from the alcs. and dry HCl (refluxing 2-3 hrs.): Me m.

223-4°, 63%; Et m. 139-40°, 60%; Pr m. 105.5-7°, 85%;

iso-Am m. 126.5-7.5°, 77%; allyl (?) m. 112.5-13.5°, 51%;

2-hydroxyethyl m. 127-8°, 60%; benzyl m. 160-1°, 73%; Ph

(prepared from the acid chloride of I and PhOH in C<sub>2</sub>Cl<sub>4</sub> and C<sub>5</sub>H<sub>5</sub>N) m.

226-7°, 39%. The amide of I m. 255.5-6.5° (decomposition); the

Et ester and 33% aqueous EtNH<sub>2</sub> for 10 days at room temperature give the ethylamide,

m. 247-8° (decomposition); the acid chloride and 2 equivs. of amine give

the diethylamide, m. 223-3.5°; the morpholide, m. 168-70°,

resolidifies and then m. 255.5-7°; the anilide m. 269-70°.

BzCH<sub>2</sub>CN (14.5 g.), 13 g. KCN and 45.5 g. (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> in 65% EtOH, heated 24 hrs. at 58-62°, give 9% (51% on nitrile not recovered) of

5-phenyl-5-hydantoinacetonitrile, m. 251.5-2.5° (decomposition).

5-Phenyl-5-(1-cyanoethyl)hydantoin could not be prepared from MeBzCHCN.

MeCHBzCO<sub>2</sub>Et, KCN and (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> give 32% of 5-phenyl-5-(1-

carbethoxyethyl)hydantoin, m. 241-2°; hydrolysis with 1:1 HCl gives

84% of the free acid, m. 271.5-3°.

IT 858786-58-0, 5-Hydantoinacetamide, 5-phenyl- 858786-60-4

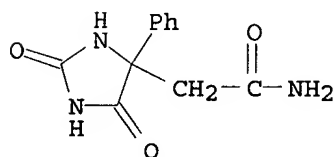
, 5-Hydantoinacetamide, N-ethyl-5-phenyl- 858786-61-5,

5-Hydantoinacetamide, N,N-diethyl-5-phenyl-

(preparation of)

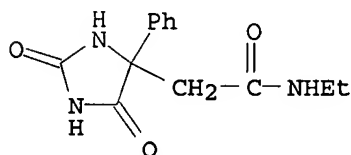
RN 858786-58-0 CAPLUS

CN 5-Hydantoinacetamide, 5-phenyl- (4CI) (CA INDEX NAME)



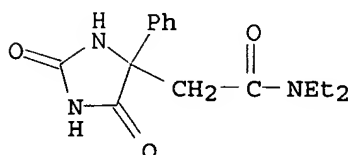
RN 858786-60-4 CAPLUS

CN 5-Hydantoinacetamide, N-ethyl-5-phenyl- (4CI) (CA INDEX NAME)



RN 858786-61-5 CAPLUS

CN 5-Hydantoinacetamide, N,N-diethyl-5-phenyl- (4CI) (CA INDEX NAME)



L5 ANSWER 87 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1937:3033 CAPLUS

DOCUMENT NUMBER: 31:3033

ORIGINAL REFERENCE NO.: 31:401h-i,402a-i,403a-b

TITLE: Synthesis of dehydracetic acid from acetoacetic ester

AUTHOR(S): Arndt, F.; Eistert, B.; Scholz, H.; Aron, E.

SOURCE: Ber. (1936), 69B, 2373-80

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

OTHER SOURCE(S): CASREACT 31:3033

AB Unexpected lack of success has frequently been experienced, both in Arndt's laboratory (Breslau) and elsewhere, in the application of the method of preparing dehydracetic acid (I) described some yrs. ago (A. and Nachtwey, C. A. 19, 286). Systematic investigations were accordingly undertaken, simultaneously and independently, at the Breslau laboratory and the main

laboratory of

the I. G. Farbenindustrie A.-G. to determine the cause of these difficulties.

The results of these investigations are reported jointly in this paper.

The trouble has been traced to the material of which the reaction vessels were made. The reaction has to be catalyzed by min. amts. of alkali. In

the original expts. of A. and N. and in many later ones, the glass used furnished this necessary alkali, but with improvements in the manufacture of laboratory glassware, this source of alkali was eliminated. It is most

reliably

supplied by the addition of min. amts. of  $\text{NaHCO}_3$ ; glass wool, borax, soft enamel and the like can also be used, although with less favorable results. The length of boiling required for the reaction can be more or less decreased according to the amount of alkali added, but the latter must be kept within very narrow limits for it not only catalyzes the formation of I but also a decomposition of the  $\text{AcCH}_2\text{CO}_2\text{Et}$  (II) to acetone. Thus, with 0.05 g.  $\text{NaHCO}_3$  the cleavage of 70 g. alc. from 300 g. II can be effected in 4 h. instead of the 8 h. reported by A. and N. but the yield of I (based on the II used up) is only 60% as against their 80%. Where yield is more important than time, it is better to use a smaller amount of alkali (0.001% or less of the weight of II) and when, after about 4 h., approx. 25% of the theor. amount of alc. has distilled over, to distill off all the II still present and use it for another charge. In this way, 80-90% yields of I can now again be obtained. The crude I so prepared is already pure enough, after being pressed, for many purposes; it can readily be further purified by dissolving it in dilute  $\text{Na}_2\text{CO}_3$ , boiling with charcoal and reprecipitating with acid. It is best obtained entirely pure and snow-white by distillation in vacuo and subsequent crystallization from alc., although this

involves

losses. As pointed out by A. and N., the cardinal point in the process is the continuous removal of the liberated alc. This has been shown even more convincingly in expts. in which II was heated to its boiling temperature and higher in sealed tubes; even with alkali and after long heating, practically no I was formed. The mechanism of the reaction originally suggested is still believed to be correct:  $2\text{II} \xrightarrow{\text{EtOH} + \text{MeC}(\text{CH}_3)_2\text{CO}_2\text{Et}} \text{OCOCH}_2\text{Ac} \rightarrow \text{I} + \text{EtOH}$ . It is the 2nd, irreversible reaction (a Claisen condensation) which requires the alkali for its catalysis. This view has been further confirmed by a study of the so-called thermal condensation of II. According to Oppenheim and Precht (Ber. 9, 324(1876)), the vapor of II passed through an Fe tube filled with pumice and heated to nearly dark redness gives I, although in varying, always moderate yields and in impure state, and the tube soon becomes stopped up by the formation of coke. The present authors studied the influence of various other substances on the vapor of II at 300-600°. Quartz, Al, Cu and V2A steel had no effect on the vapor; glass or porcelain in the absence of Fe (best in tubes of the same

material), on the other hand, gave pure snow-white I in good yields as long as the temperature was not raised higher than about 400°; about 25% of the II was thus transformed. The process can be continued a long time without plugging up of the tube. The formation of "dehydro acids" from  $\beta$ -keto esters is not limited to II. With the experience gained in the work on II there is now available a practical method of preparing I and other dehydro acids which hitherto could be obtained only as byproducts and with uncertainty. The dehydro acids are of importance in that various pyrone and pyridine derivs. can be readily prepared from them; some examples of such reactions are given. Thus, 70 g. crude I boiled with 200 cc. concentrated HCl until foaming ceases, then evaporated to dryness on the water

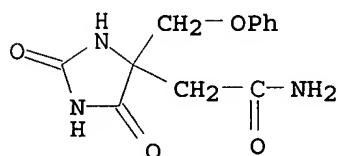
bath

and crystallized 3 times from pyridine, gives 33 g. almost pure 2,6-dimethylpyrone. 6-Methylpyronone (from I and 90% H<sub>2</sub>SO<sub>4</sub> at 135°) with aqueous MeNH<sub>2</sub> at 30° gives 1,6-dimethyl-4-hydroxy-2-pyridone, decomposing 225-6° (120-5 g. from 130 g. pyronone). 1-Ethyl-6-Me homolog, similarly prepared with EtNH<sub>2</sub>, decomps. 198°. 1-Cyclohexyl-6-Me compound, m. 108°. 1-(p-Dimethylaminophenyl)-6-Me der., decomps. 270-5°. With PhNH<sub>2</sub> the methylpyronone undergoes extensive decomposition, yielding a product, m. 199-200°, which does not have the properties expected of a hydroxypyridone; it is not soluble in NaOH without decomposition and does not couple with diazo compds. Dehydrobenzoylacetic acid, m. 171°, is obtained in 90-110 g. yield from 150 g. BzCH<sub>2</sub>CO<sub>2</sub>Et diluted with 150 cc. o-C<sub>6</sub>H<sub>4</sub>Cl<sub>2</sub> boiled with a trace of NaHCO<sub>3</sub> until about 20 cc. alc. has distilled over; 50 g. of this acid added with stirring to a cold mixture of 30 cc. water and 300 cc. concentrated H<sub>2</sub>SO<sub>4</sub>, then heated as rapidly as possible to 138-40° (by immersing the flask in an oil bath at 160°), kept 1 min. at this temperature, and quickly cooled in ice water, gives 6-phenylpyronone as a brownish, sandy crystalline powder, decomposing 245-6°, which with aqueous NH<sub>4</sub>OH at 120° yields 2,4-dihydroxy-6-phenylpyridine, decomposing 315-18°.

IT 873421-97-7, 5-Hydantoinacetamide, 5-phenoxyethyl-  
(preparation of)

RN 873421-97-7 CAPLUS

CN 5-Hydantoinacetamide, 5-phenoxyethyl- (4CI) (CA INDEX NAME)



L5 ANSWER 88 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1936:57003 CAPLUS

DOCUMENT NUMBER: 30:57003

ORIGINAL REFERENCE NO.: 30:7542f-h

TITLE: Condensation of ethyl  $\beta$ -methyladipate with ethyl oxalate

AUTHOR(S): Broun, A. S.

SOURCE: Zhurnal Obshchei Khimii (1936), 6, 612-15

CODEN: ZOKHA4; ISSN: 0044-460X

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB Naumov (unpublished work) condensed (CH<sub>2</sub>)<sub>4</sub>(CO<sub>2</sub>Et)<sub>2</sub> with (CO<sub>2</sub>Et)<sub>2</sub> (I) in the presence of Na and a little alc., obtaining about 50% di-Et cyclohexane-2,3-dione-1,4-dicarboxylate, m. 53-4°. A mixture of 54

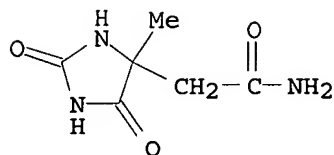


g. Na, 97 g. I and 15 cc. absolute EtOH was treated dropwise with 126 g. Et  $\beta$ -methyladipate and stirring continued for 4 hrs. After standing overnight, the reaction mixture on the addition of absolute Et<sub>2</sub>O was refluxed at 40° for 7-8 hrs., giving di-Et 6-methylcyclohexane-2,3-dione-1,4-dicarboxylate, b<sub>15</sub> 206-7°.

IT 876479-33-3, 5-Hydantoinacetamide, 5-methyl-  
(preparation of)

RN 876479-33-3 CAPLUS

CN 5-Hydantoinacetamide, 5-methyl- (3CI) (CA INDEX NAME)



L5 ANSWER 89 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1936:57004 CAPLUS

DOCUMENT NUMBER: 30:57004

ORIGINAL REFERENCE NO.: 30:7542h-i

TITLE: Preparation and resolution of homoaspartic acid

AUTHOR(S): Pfeiffer, Paul; Heinrich, Ernst

SOURCE: Journal fuer Praktische Chemie (Leipzig) (1936), 146, 105-12  
CODEN: JPCEAO; ISSN: 0021-8383

DOCUMENT TYPE: Journal

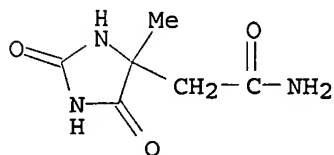
LANGUAGE: Unavailable

AB Heating 13 g. AcCH<sub>2</sub>CO<sub>2</sub>Et, 20 g. (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> and 12 g. KCN in 60 cc. 50% EtOH under 20 atmospheric pressure of CO<sub>2</sub> 5 hrs. at 70-80° gives Et 5-methylhydantoin-5-acetate, m. 138° (amide, m. 252° (decomposition); hydrazide, m. 104-5°); heating 5 g. ester with 75 cc. 40% KOH for 48 hrs. gives homoaspartic acid (I), m. 233° (decomposition); HCl salt, m. 212° (decomposition); Ca salt, with 3 mols. H<sub>2</sub>O; Ba salt, with 4 mols. H<sub>2</sub>O; Pb salt, with 2 mols. H<sub>2</sub>O; Cu salt, with 3 mols. H<sub>2</sub>O diamide, from the crude di-Me ester, m. 173°; Ac derivative, m. 156-7°. I in H<sub>2</sub>O yields a strychnine salt, with 2 mols. H<sub>2</sub>O, m. 240° (decomposition),  $\alpha$ <sub>D</sub><sup>24</sup> -28.67°; with N NaOH this yields a I with  $[\alpha]$ <sub>D</sub><sup>20</sup> 3.55°; the filtrate gives the l-I,  $[\alpha]$ <sub>D</sub><sup>20</sup> -3.47°.

IT 876479-33-3, 5-Hydantoinacetamide, 5-methyl-  
(preparation of)

RN 876479-33-3 CAPLUS

CN 5-Hydantoinacetamide, 5-methyl- (3CI) (CA INDEX NAME)

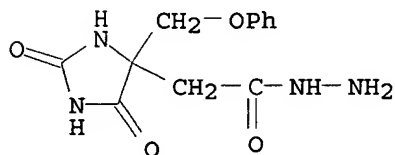


L5 ANSWER 90 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

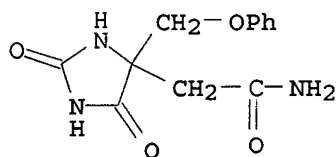
ACCESSION NUMBER: 1937:3034 CAPLUS  
 DOCUMENT NUMBER: 31:3034  
 ORIGINAL REFERENCE NO.: 31:403b-c  
 TITLE: Synthesis of 3-hydroxychromanon-3-acetic acid  
 AUTHOR(S): Pfeiffer, Paul; Heinrich, Ernst  
 SOURCE: Journal fuer Praktische Chemie (Leipzig) (1936), 147, 93-8  
 CODEN: JPCEAO; ISSN: 0021-8383  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Unavailable  
 AB Et 5-phenoxyethylhydantoin-5-acetate (I) forms an amide, m. 232°, and a hydrazide, m. 178°. Alkaline hydrolysis of I, followed by HNO<sub>2</sub>, gives γ-phenoxyphenylmalic acid, PhOCH<sub>2</sub>C(OH)(CO<sub>2</sub>H)CH<sub>2</sub>CO<sub>2</sub>H (II), which forms an amide, m. 183-4°. II and AcCl, heated 4 hrs., give the anhydride (III) of II, m. 92°; NH<sub>4</sub>OH gives the salt PhOCH<sub>2</sub>C(OH)(CONH<sub>2</sub>)CH<sub>2</sub>CO<sub>2</sub>NH<sub>4</sub> or PhOCH<sub>2</sub>C(OH)(CO<sub>2</sub>NH<sub>4</sub>)CH<sub>2</sub>CONH<sub>2</sub>. III and AlCl<sub>3</sub> at 115-20° for 8 hrs. give 3-hydroxychromanon-3-acetic acid, an oil; Ba salt. α-Phenoxyethylacetylaspartic anhydride, from the aspartic acid and AcCl; ester acid, m. 222-3°.

IT 858786-42-2, 5-Hydantoinacetic acid, 5-phenoxyethyl-, hydrazide  
 873421-97-7, 5-Hydantoinacetamide, 5-phenoxyethyl-  
 (preparation of)

RN 858786-42-2 CAPLUS  
 CN 5-Hydantoinacetic acid, 5-phenoxyethyl-, hydrazide (4CI) (CA INDEX NAME)



RN 873421-97-7 CAPLUS  
 CN 5-Hydantoinacetamide, 5-phenoxyethyl- (4CI) (CA INDEX NAME)



L5 ANSWER 91 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1936:22334 CAPLUS  
 DOCUMENT NUMBER: 30:22334  
 ORIGINAL REFERENCE NO.: 30:2925h-i,2926a  
 TITLE: A new method for forming hydantoic compounds  
 AUTHOR(S): Jerzmanowska-Sienkiewiczowa, Z.  
 SOURCE: Roczniki Chemii (1935), 15, 202-8  
 CODEN: ROCHAC; ISSN: 0035-7677  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Unavailable  
 GI For diagram(s), see printed CA Issue.  
 AB Condensation of urea with Et maleate or fumarate results in 2 products: hydantoinacetic acid (I) and its ureide (II). I results from a partial

hydrolysis of II. The reaction proceeds thus:  $\text{EtCO}_2\text{CH:CHCO}_2\text{Et} \rightarrow \text{EtCO}_2\text{CH:CHCONHCONH}_2 \rightarrow \text{CO.NH.CO.NH.CH CH}_2\text{CO}_2\text{Et} \rightarrow \text{CO.NH.CO.NH.CHCH}_2\text{CONHCONH}_2$ . 10.4 g. urea is added to 4 g. Na in 100 cc. anhydrous alc., heated until solution results and maintained at 75°, then 10 g. of the maleate (1 mole) or the fumarate (in proper ratio) is added. Heating is carried on 15 min. after the formation of a copious precipitate

After

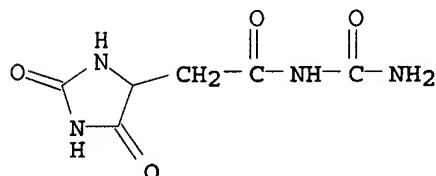
cooling, filtering and washing with alc., the precipitate, dissolved in water and

strongly acidified with 20% HCl, gives 36-40% of crystals of II, m. 273-4°. The filtrate after the separation of crude II is evaporated and the oily residue, after washing with cold alc., is extracted in a Soxhlet with  $\text{Me}_2\text{CO}$ , giving 10-12% of I, m. 213-14°.

IT 198337-26-7, 5-Hydantoinacetic acid, ureide  
(preparation of)

RN 198337-26-7 CAPLUS

CN 4-Imidazolidineacetamide, N-(aminocarbonyl)-2,5-dioxo- (9CI) (CA INDEX NAME)



L5 ANSWER 92 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1933:53514 CAPLUS

DOCUMENT NUMBER: 27:53514

ORIGINAL REFERENCE NO.: 27:4789d-f

TITLE: Brazilin and hematoxylin question. XIII.  
Phenoxycitramalic acid

AUTHOR(S): Pfeiffer, P.; Hoyer, H.

SOURCE: Journal fuer Praktische Chemie (Leipzig) (1933), 138, 69-80

CODEN: JPCEAO; ISSN: 0021-8383

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB cf. C. A. 27, 3940. The following is an improved method for preparing 3-MeOC<sub>6</sub>H<sub>4</sub>OCH<sub>2</sub>C(OH)(CO<sub>2</sub>H)CH<sub>2</sub>CO<sub>2</sub>H (I) (cf. C. A. 23, 4480).

3-Methoxyphenoxyacetamide, m. 110°, results in 3 g. yield from 6 g.

3-MeOC<sub>6</sub>H<sub>4</sub>OCH<sub>2</sub>COCH(CN)CO<sub>2</sub>Et, KCN and (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub> in 50% EtOH heated 5 hrs. at 80-90°. 3-MeOC<sub>6</sub>H<sub>4</sub>OCH<sub>2</sub>COCH<sub>2</sub>CO<sub>2</sub>Et, KCN and (NH<sub>4</sub>)<sub>2</sub>CO<sub>3</sub>, heated in 50%

EtOH under 10 atmospheric CO<sub>2</sub> 5 hrs. at 80-90°, give Et

5-(3-methoxyphenoxyethyl)hydantoin-5-acetate, m. 133-4°; concentrated

NH<sub>4</sub>OH gives the amide, m. 203-4°; boiling 25% KOH (about 18 hrs.)

gives α-(3-methoxyphenoxyethyl)aspartic acid, m. about 170°

(decomposition); Ba salt, crystals with 1 mol. H<sub>2</sub>O; HNO<sub>2</sub> gives I; Ba salt, crystals with 1 mol. H<sub>2</sub>O. Et 5-phenoxyethylhydantoin-5-acetate, crystals

with 1 mol. H<sub>2</sub>O, m. 157-8°; free acid, m. 238-9°; heating

the ester with 25% KOH gives α-phenoxyethylaspartic acid, m.

230-40° (decomposition); Ba salt, crystals with 1 mol. H<sub>2</sub>O; HNO<sub>2</sub> gives

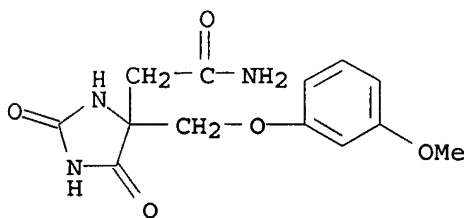
γ-phenoxyethylaspartic acid, m. 173-4°; Ba salt, crystals with 1

mol. H<sub>2</sub>O; di-Me ester, m. 67-8°.

IT 857795-83-6, 5-Hydantoinacetamide, 5-[(m-methoxyphenoxy)methyl]-  
(preparation of)

RN 857795-83-6 CAPLUS

CN 5-Hydantoinacetamide, 5-[(m-methoxyphenoxy)methyl]- (3CI) (CA INDEX NAME)



L5 ANSWER 93 OF 93 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1912:22088 CAPLUS

DOCUMENT NUMBER: 6:22088

ORIGINAL REFERENCE NO.: 6:3091b-d

TITLE: Hydantoins. XIV. The Action of Potassium Thiocyanate on Asparagine

AUTHOR(S): Johnson, T. B.; Guest, H. H.

CORPORATE SOURCE: Yale Univ.

SOURCE: American Chemical Journal (1912), 48, 103-11

CODEN: ACJOAZ; ISSN: 0096-4085

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

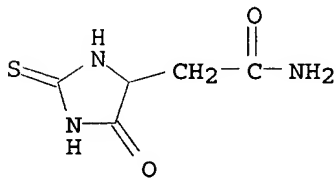
AB 3-Acetyl-2-thiohydantoin-4-acetamide(I) was prepared on heating a mixture of anhydrous asparagine and dry KCNS in the presence of Ac<sub>2</sub>O, prisms, m. 222-3°. From the filtrate, 2-thiohydantoin-4-acetamide, C<sub>5</sub>H<sub>7</sub>O<sub>2</sub>N<sub>3</sub>S, separated on evaporation. On hydrolysis of (I) with HCl,

2-thiohydantoin-4-acetic acid (II) separated, plates, m. 222°. (decompose). On digesting (II) with CH<sub>2</sub>ClCO<sub>2</sub>H, hydantoin-4-acetic acid (malyureidic acid) was obtained, blocks, m. 214-5°. Aspartic acid is deaminized by the action of KCNS in the presence of Ac<sub>2</sub>O, no thiohydantoin being formed.

IT 64419-95-0, 4-Imidazoleacetamide, tetrahydro-5-keto-2-thioketo- (preparation of)

RN 64419-95-0 CAPLUS

CN 4-Imidazolidineacetamide, 5-oxo-2-thioxo- (9CI) (CA INDEX NAME)



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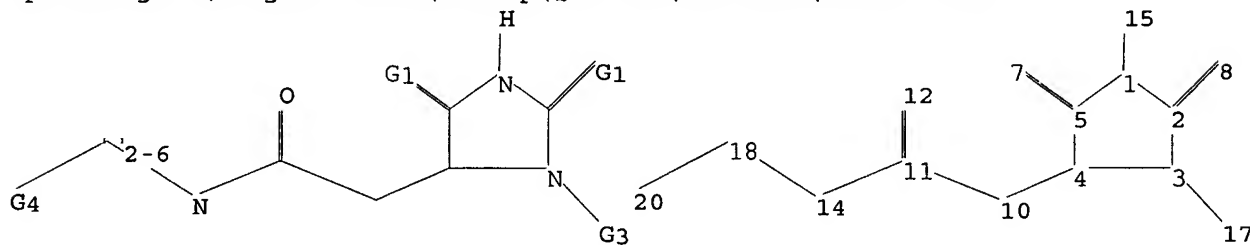
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chain nodes :  
7 8 10 11 12 14 15 17 18 20  
ring nodes :  
1 2 3 4 5

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Page 21

chain bonds :

1-15 2-8 3-17 4-10 5-7 10-11 11-14 11-12 14-18 18-20

ring bonds :

1-2 1-5 2-3 3-4 4-5

exact/norm bonds :

1-2 1-5 2-3 2-8 3-4 3-17 4-5 5-7 11-14 11-12 14-18 18-20

exact bonds :

1-15 4-10 10-11

G1:O,S

G2:C,N

G3:H,CH3

G4:Cb,Cy,Hy

Match level :

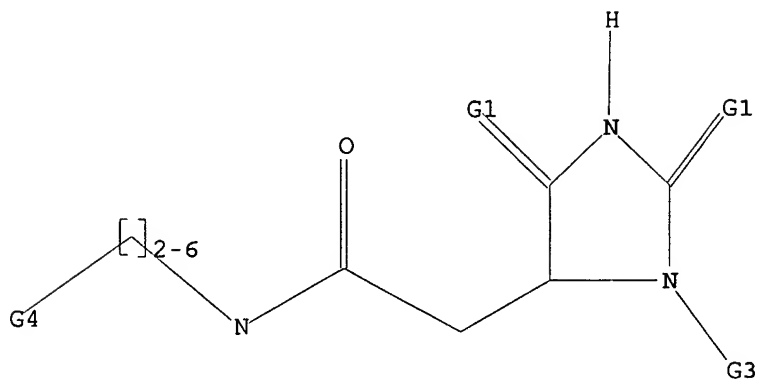
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12:CLASS 14:CLASS 15:CLASS 17:CLASS 18:CLASS 20:CLASS

L6 STRUCTURE UPLOADED

=> d

L6 HAS NO ANSWERS

L6 STR



G1 O,S

G2 C,N

G3 H,Me

G4 Cb,Cy,Hy

Structure attributes must be viewed using STN Express query preparation.

=> l6

SAMPLE SEARCH INITIATED 09:57:47 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 8 TO ITERATE

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100.0% PROCESSED 8 ITERATIONS 3 ANSWERS  
 SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
 BATCH \*\*COMPLETE\*\*  
 PROJECTED ITERATIONS: 8 TO 329  
 PROJECTED ANSWERS: 3 TO 163

L7 3 SEA SSS SAM L6

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 FULL SCREEN SEARCH COMPLETED - 184 TO ITERATE

100.0% PROCESSED 184 ITERATIONS 96 ANSWERS  
 SEARCH TIME: 00.00.01

L8 96 SEA SSS FUL L6

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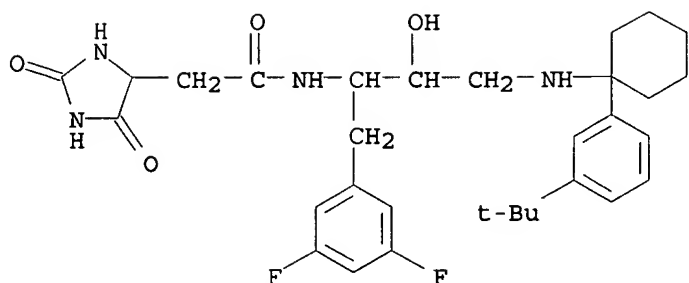
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L9 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2005:1021606 CAPLUS  
 DOCUMENT NUMBER: 143:326096  
 TITLE: Preparation of substituted urea and carbamate,  
 phenacyl-2-hydroxy-3-diaminoalkane, and  
 benzamide-2-hydroxy-3-diaminoalkane aspartyl protease  
 and  $\beta$ -secretase inhibitors for treating  
 conditions associated with amyloidosis such as  
 Alzheimer's disease  
 INVENTOR(S): John, Varghese; Maillard, Michel; Tucker, John;  
 Aquino, Jose; Hom, Roy; Tung, Jay; Dressen, Darren;  
 Shah, Neerav; Neitz, R. Jeffrey  
 PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 532 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005087215	A1	20050922	WO 2005-US7775	20050309
W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW	
RW:			BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG	
US 2005261273	A1	20051124	US 2005-75292	20050309
PRIORITY APPLN. INFO.:			US 2004-551192P	P 20040309
			US 2004-575829P	P 20040602
			US 2004-591857P	P 20040729
			US 2004-622589P	P 20041028
OTHER SOURCE(S):		MARPAT 143:326096		
AB		The invention is related to compds. of formula R2NHCH(R1)CH(OH)CH2NHRc (I) [R1 = (un)substituted benzyl, thien-2-ylmethyl, etc.; R2 = NH2 and derivs., SO2-aryl, hetero/aryl-U, etc.; U = CO, CS, CONH and derivs., etc.; Rc = carbocyclyl or heterocyclyl; with addnl. details given in the claims] particularly acetyl 2-hydroxy-1,3-diaminospirocyclohexanes and derivs., that are useful in treating diseases, disorders, and conditions associated with amyloidosis. Amyloidosis refers to a collection of diseases, disorders, and conditions associated with abnormal deposition of A- $\beta$ protein. For example, alkylation of (2R,3S)-3-amino-1-[[1-(3-tert-butylphenyl)cyclohexyl]amino]-4-(3,5-difluorophenyl)butan-2-ol•2HCl with 4-iodobenzamide gave the coresponding amide. Selected I displayed IC50 values < 5 $\mu$ M in a cell free inhibition assay utilizing a synthetic APP substrate that can be cleaved by $\beta$ -secretase. The selectivity of I for $\beta$ -secretase vs. cathepsin D for 6 examples of I are tabulated. Brain uptake, total polar surface area and/or lipophilicity for 32 examples of I are tabulated.		
IT		865375-15-1P, N-[3-[[1-(3-tert-Butylphenyl)cyclohexyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-2-(2,5-dioxoimidazolidin-4-yl)acetamide		
		RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)		
		(drug candidate; preparation of as aspartyl protease and $\beta$ -secretase inhibitors)		
RN		865375-15-1 CAPLUS		
CN		4-Imidazolidineacetamide, N-[1-[(3,5-difluorophenyl)methyl]-3-[[1-[3-(1,1-dimethylethyl)phenyl]cyclohexyl]amino]-2-hydroxypropyl]-2,5-dioxo- (9CI) (CA INDEX NAME)		





REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:612099 CAPLUS

DOCUMENT NUMBER: 143:133696

TITLE: Preparation of peptide phosphonic acid derivatives for the inhibition of undesired cell proliferation

INVENTOR(S): Knolle, Jochen; Schutkowski, Mike; Hummel, Gerd; Tradler, Thomas; Jobron, Laurence; Christner, Claudia; Gibson, Christoph; Zischinsky, Gunther

PATENT ASSIGNEE(S): Jerini A.-G., Germany

SOURCE: PCT Int. Appl., 110 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

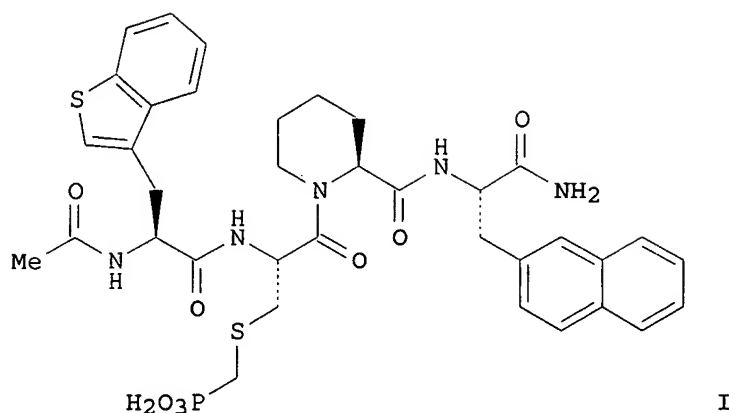
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005063259	A1	20050714	WO 2004-EP14460	20041218
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: EP 2003-29450 A 20031219

OTHER SOURCE(S): MARPAT 143:133696

GI



AB The invention relates to phosphonic acid derivs.  $R_1-X_1-P(O)(X_2-R_2)-Y-Z-W_1(A_1-R_3)(A_2-R_4)-W_2(A_3-R_5)(A_4-R_6)-W_3(A_5-R_7)(A_6-R_8)-A_7-Q(T)-V(U)-A_8-CR_9R_{10}-A_9-R_{11}$  [ $R_1, R_2$  are independently H or phospho-protecting groups;  $X_1, X_2$  are independently O, S or  $NR_{12}$ ; Z is O, S,  $NR_{13}$  or  $CR_4R_5$ ;  $A_1-A_9$  are independently null, O, S,  $NR_{16}$ , SO,  $SO_2$ , CO, C(S),  $NR_{17}CO$ ,  $NR_{18}C(S)$ ,  $NR_{19}CONR_{20}$ ,  $NR_{21}C(S)NR_{22}$ ,  $NR_{23}S(O)$ ,  $NR_{24}SO_2$  or  $NR_{25}CO_2$ ; Y is O or  $CR_{26}R_{27}$ ; Q, V are independently  $CR_{28}$  or N;  $W_1, W_2, W_3$  are independently C or N;  $R_3-R_{28}, T, U$  are independently null, H, halo, (un)substituted alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, etc.; or T and U may be connected by a single or double bond] and to pharmaceutical compns. containing the compds. for the treatment of diseases involving abnormal or undesired cell proliferation or mitosis. Thus, peptide phosphonic acid derivative I, prepared via peptide coupling in the solid phase, was a potent rotamase inhibitor ( $IC_{50} < 1 \mu M$ ).

IT **858352-64-4P 858648-24-5P**

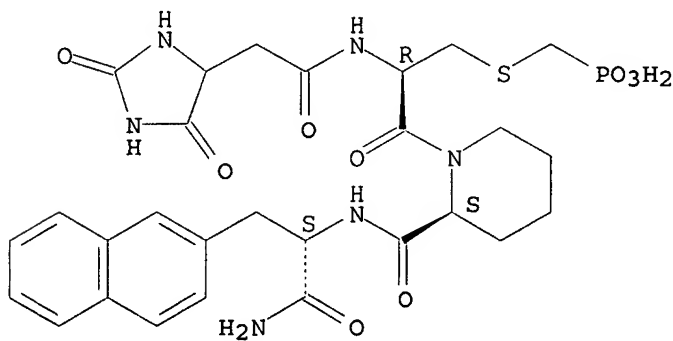
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptide phosphonic acid derivs. for inhibition of undesired cell proliferation)

RN 858352-64-4 CAPLUS

CN L-Alaninamide, N-[(2,5-dioxo-4-imidazolidinyl)acetyl]-S-(phosphonomethyl)-L-cysteiny-(2S)-2-piperidinecarbonyl-3-(2-naphthalenyl)- (9CI) (CA INDEX NAME)

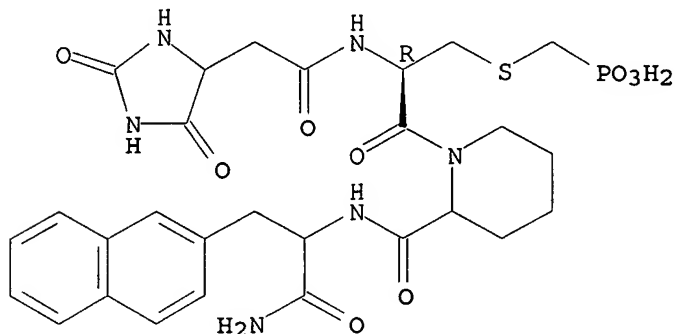
Absolute stereochemistry.



RN 858648-24-5 CAPLUS

CN Phosphonic acid, [[[(2R)-3-[2-[[[2-amino-1-(2-naphthalenylmethyl)-2-oxoethyl]amino]carbonyl]-1-piperidinyl]-2-[[2,5-dioxo-4-imidazolidinyl]acetyl]amino]-3-oxopropyl]thio]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:701970 CAPLUS

DOCUMENT NUMBER: 141:225511

TITLE: Preparation of substituted azoles as protein tyrosine phosphatase inhibitors for treatment of diabetes and other PTPase mediated conditions

INVENTOR(S): Mjalli, Adnan M. M.; Andrews, Robert C.; Yarragunta, Ravindra R.; Xie, Rongyuan; Ren, Tan; Subramanian, Govindan; Quada, James C., Jr.

PATENT ASSIGNEE(S): Transtech Pharma Inc., USA

SOURCE: PCT Int. Appl., 224 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

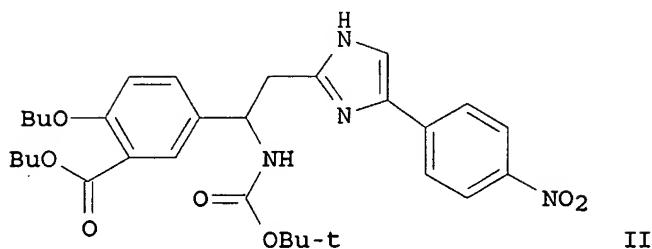
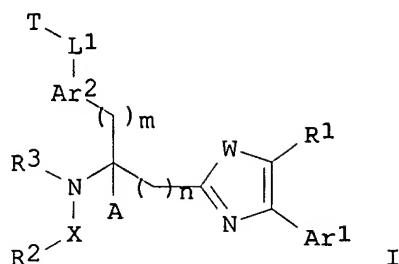
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004071448	A2	20040826	WO 2004-US4076	20040212
WO 2004071448	A3	20041014		
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

US 2004186151 A1 20040923 US 2004-777471 20040212

PRIORITY APPLN. INFO.: US 2003-446924P P 20030212

OTHER SOURCE(S):  
GI

MARPAT 141:225511



AB Title imidazoles and analogs I [wherein m, n = independently 0, 1; A = H, alkyl, alkenyl, alkynyl; L1 = a bond, O, alkylene, CO, NHCO, NH, NHSO<sub>2</sub>, etc.; T = H, (un)substituted (cyclo)alkyl, heterocyclyl, (hetero)aryl, etc.; W = O, S, NR<sub>4</sub>; X = a bond, CO, CH<sub>2</sub>, SO<sub>2</sub>; R<sub>1</sub> = H, halo, CN, alkyl, (hetero)aryl, heterocyclyl, etc.; R<sub>2</sub> = H, perfluoroalkyl, alkylene optionally interrupted by one or more heteroatoms, (hetero)aryl, heterocyclyl, etc.; R<sub>3</sub> = H, alkyl, (cyclo)alkylalkylene, (hetero)aryl(alkylene); R<sub>4</sub> = H, alkyl, (hetero)aryl(alkyl), heterocyclyl(alkyl), etc.; Ar<sub>1</sub> = (un)substituted optionally fused (hetero)aryl; Ar<sub>2</sub> = (un)substituted optionally fused (hetero)arylene; and pharmaceutically acceptable salts, solvates, and prodrugs thereof] were prepared as inhibitors of protein tyrosine phosphatases (PTPases). For example, 3-[(tert-butoxycarbonyl)amino]-2-(4-butoxy-3-butoxycarbonylphenyl)-2-ethyl-4-(4-nitrophenyl)imidazole was coupled with 4-nitrophenacyl bromide to give the keto ester, which was treated with ammonium acetate in glacial acetic acid/anhydrous DMF to afford the imidazole II (40%). Comps. of the invention inhibited PTP 1B activity with IC<sub>50</sub> values ranging from about 0.01  $\mu$ M to about 20  $\mu$ M. Thus, I and pharmaceutical comps. comprising them may be useful for the management, treatment, control, and adjunct treatment of diseases mediated by PTPase activity, such as Type I diabetes, Type II diabetes, immune dysfunction, AIDS, autoimmune diseases, glucose intolerance, obesity, cancer, psoriasis, allergic diseases, infectious diseases, inflammatory diseases, diseases involving the modulated synthesis and/or production of growth hormone or cytokines, of Alzheimer's disease (no data).

IT 745834-40-6P

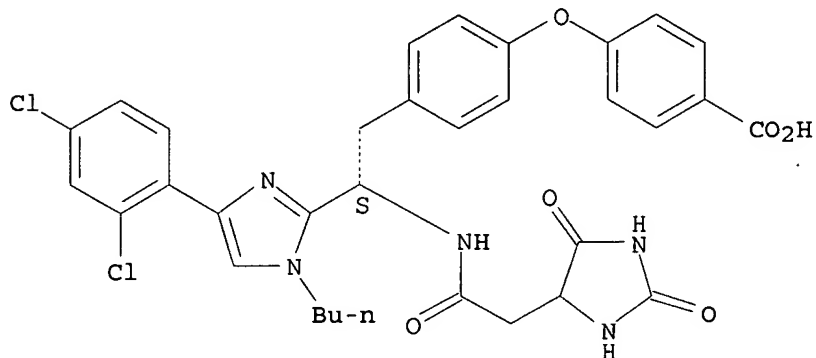
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PTPase inhibitor; preparation of substituted imidazoles as PTPase inhibitors for treatment of diabetes and other PTPase mediated conditions)

RN 745834-40-6 CAPLUS

CN Benzoic acid, 4-[4-[(2S)-2-[1-butyl-4-(2,4-dichlorophenyl)-1H-imidazol-2-yl]-2-[[2,5-dioxo-4-imidazolidinyl)acetyl]amino]ethyl]phenoxy]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

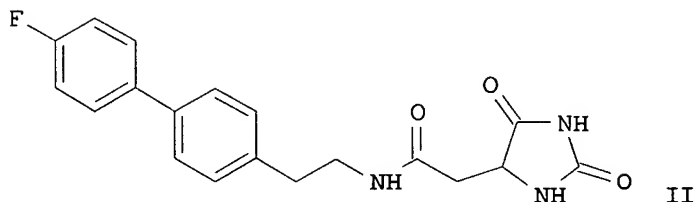
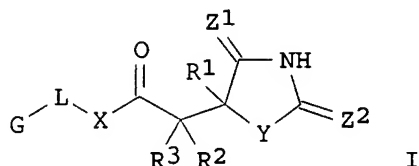


L9 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2004:203815 CAPLUS  
 DOCUMENT NUMBER: 140:235715  
 TITLE: Preparation of 2,5-dioxoimidazolidin-4-yl acetamide derivatives as inhibitors of metalloproteinase MMP12  
 INVENTOR(S): Henriksson, Krister; Munck Af Rosenschoeld, Magnus  
 PATENT ASSIGNEE(S): Astrazeneca AB, Swed.  
 SOURCE: PCT Int. Appl., 87 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020415	A1	20040311	WO 2003-SE1328	20030826
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2495853	AA	20040311	CA 2003-2495853	20030826
AU 2003253557	A1	20040319	AU 2003-253557	20030826
BR 2003013635	A	20050621	BR 2003-13635	20030826
EP 1542977	A1	20050622	EP 2003-791528	20030826
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2006503019	T2	20060126	JP 2004-532506	20030826
US 2005245586	A1	20051103	US 2005-525640	20050225
NO 2005001540	A	20050323	NO 2005-1540	20050323
PRIORITY APPLN. INFO.:			SE 2002-2539	A 20020827
			WO 2003-SE1328	W 20030826

OTHER SOURCE(S):  
GI

CASREACT 140:235715; MARPAT 140:235715



AB The title compound I [X= O, CH<sub>2</sub>, or (substituted)amino; Y = NH or N-Me; Z<sub>1</sub>, Z<sub>2</sub> = each represent an oxygen or sulfur atom, with the proviso that at least one of Z<sub>1</sub>, Z<sub>2</sub> represents an oxygen atom; R<sub>1</sub> = H, alkyl, (un)saturated 3-10 membered ring system which may comprise at least one ring heteroatom selected from nitrogen, oxygen and sulfur, etc.; R<sub>2</sub>, R<sub>3</sub> = H or C<sub>1</sub>-C<sub>6</sub> alkyl; R<sub>1</sub>/R<sub>2</sub> or R<sub>2</sub>/R<sub>3</sub> together with carbons atoms to which they are attached form a saturated 5-6 membered ring; L = -CH<sub>2</sub>C(O)-, -C(O)CH<sub>2</sub>-, alkyl, alkylene, alkynyl, etc.; G = (un)saturated 5-10 membered ring system which may comprise at least one ring heteroatom selected from nitrogen, oxygen and sulfur, etc.] were prepared as inhibitors of metalloproteinase MMP12 for the treatment of obstructive airways diseases. Thus, reaction of 5-hydantoin acetic acid with ((4'-fluorobiphenyl-4-yl)ethyl)amine yielded compound II. The latter inhibits human MMP12 with an IC<sub>50</sub> = 0.22 μM.

IT 669013-57-4P 669013-58-5P 669013-60-9P  
669013-61-0P 669013-62-1P 669013-63-2P  
669013-64-3P 669013-65-4P 669013-66-5P  
669013-67-6P 669013-68-7P 669013-69-8P  
669013-70-1P 669013-72-3P 669013-74-5P  
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669014-56-6P 669014-57-7P 669014-58-8P

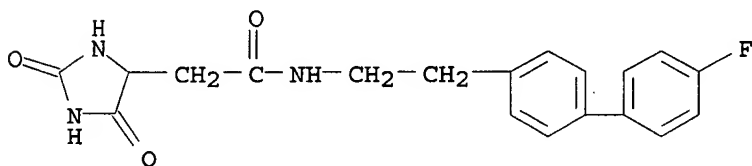
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 669014-94-2P 669014-95-3P 669014-96-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(preparation of 2,5-dioxoimidazolidin-4-yl acetamide derivs. as inhibitors  
 of metalloproteinase MMP12)

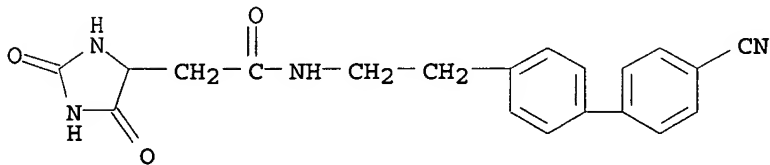
RN 669013-57-4 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-fluoro[1,1'-biphenyl]-4-yl)ethyl]-2,5-  
 dioxo- (9CI) (CA INDEX NAME)



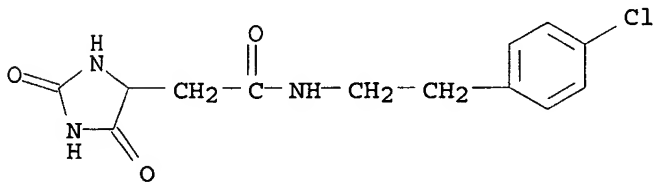
RN 669013-58-5 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-cyano[1,1'-biphenyl]-4-yl)ethyl]-2,5-  
 dioxo- (9CI) (CA INDEX NAME)



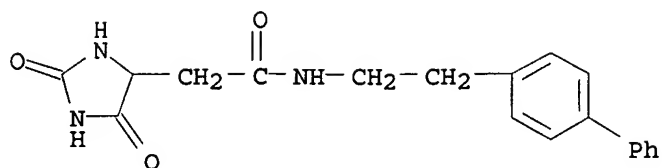
RN 669013-60-9 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4-chlorophenyl)ethyl]-2,5-dioxo- (9CI)  
 (CA INDEX NAME)



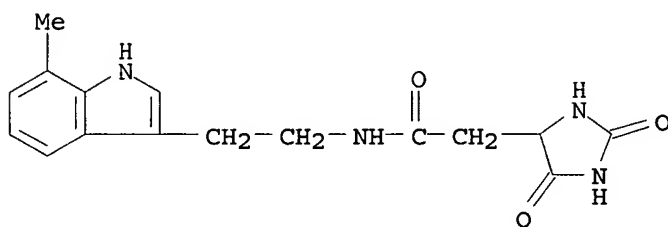
RN 669013-61-0 CAPLUS

CN 4-Imidazolidineacetamide, N-(2-[1,1'-biphenyl]-4-ylethyl)-2,5-dioxo- (9CI)  
 (CA INDEX NAME)



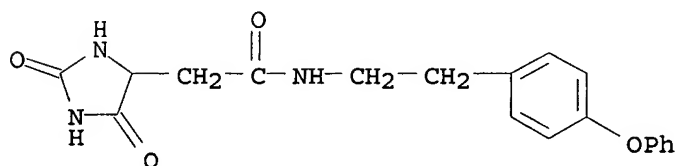
RN 669013-62-1 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(7-methyl-1H-indol-3-yl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



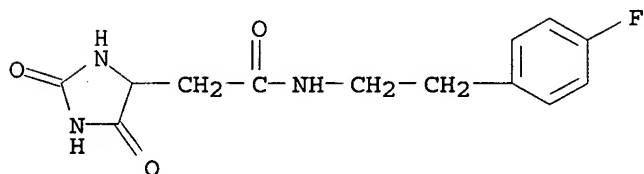
RN 669013-63-2 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-(4-phenoxyphenyl)ethyl]- (9CI) (CA INDEX NAME)



RN 669013-64-3 CAPLUS

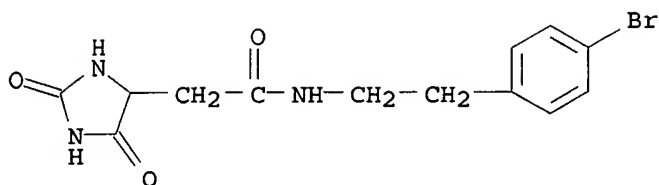
CN 4-Imidazolidineacetamide, N-[2-(4-fluorophenyl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



RN 669013-65-4 CAPLUS

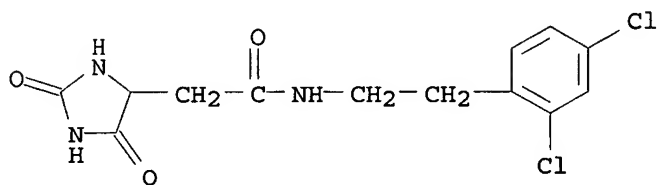
CN 4-Imidazolidineacetamide, N-[2-(4-bromophenyl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)





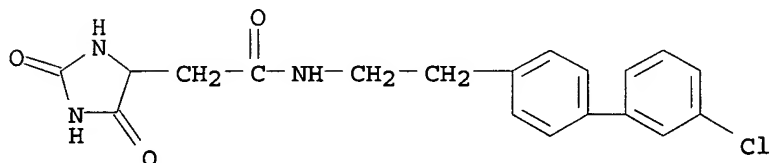
RN 669013-66-5 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(2,4-dibromophenyl)ethyl]-2,5-dioxo- (9CI)  
(CA INDEX NAME)



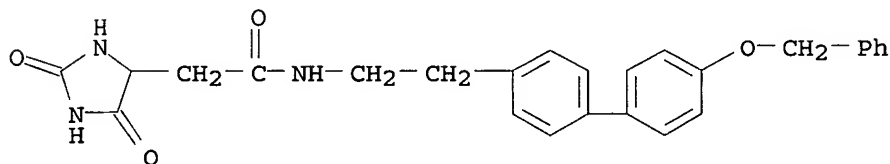
RN 669013-67-6 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3'-chloro[1,1'-biphenyl]-4-yl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



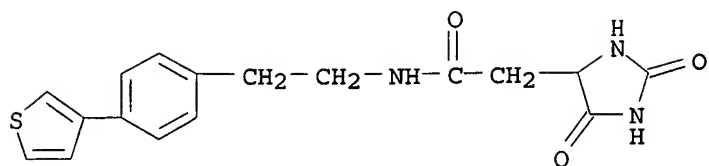
RN 669013-68-7 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4'-(phenylmethoxy)[1,1'-biphenyl]-4-yl]ethyl]- (9CI) (CA INDEX NAME)



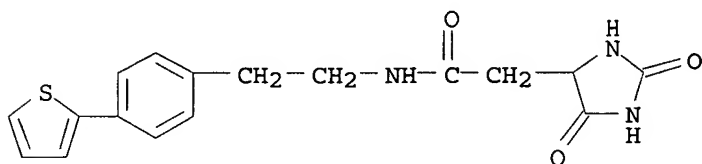
RN 669013-69-8 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4-(3-thienyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



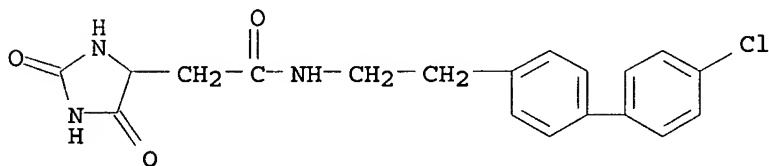
RN 669013-70-1 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4-(2-thienyl)phenyl]ethyl]-  
(9CI) (CA INDEX NAME)



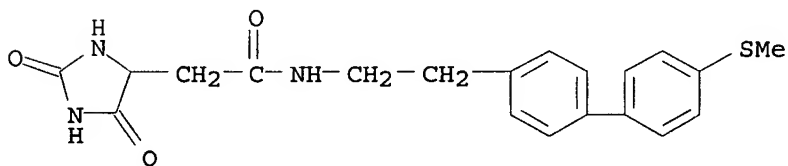
RN 669013-72-3 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-chloro[1,1'-biphenyl]-4-yl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



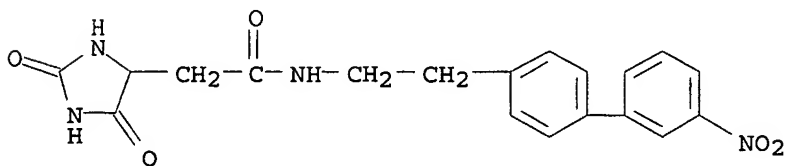
RN 669013-74-5 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-(methylthio)[1,1'-biphenyl]-4-yl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



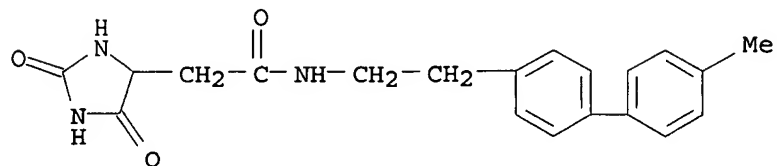
RN 669013-76-7 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3'-nitro[1,1'-biphenyl]-4-yl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



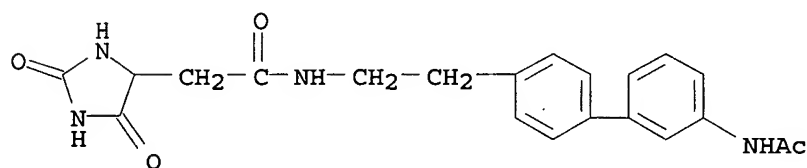
RN 669013-77-8 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-methyl[1,1'-biphenyl]-4-yl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



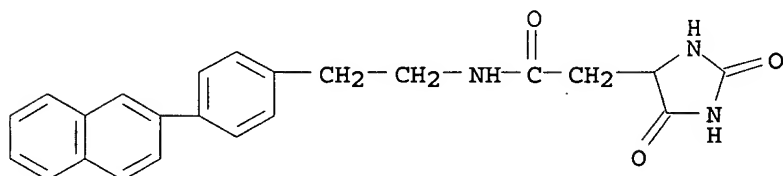
RN 669013-78-9 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[3'-(acetylamino)[1,1'-biphenyl]-4-yl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



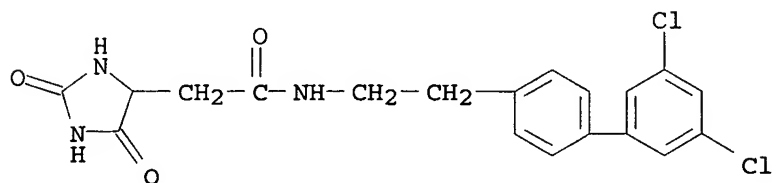
RN 669013-79-0 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(2-naphthalenyl)phenyl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



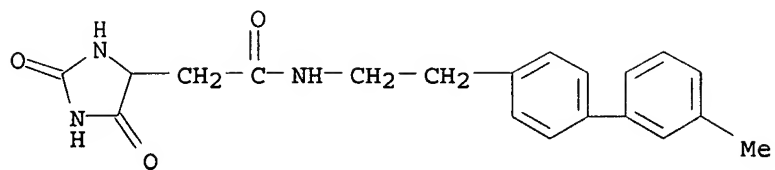
RN 669013-80-3 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3',5'-dichloro[1,1'-biphenyl]-4-yl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



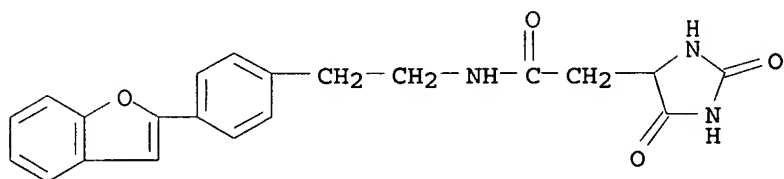
RN 669013-82-5 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3'-methyl[1,1'-biphenyl]-4-yl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



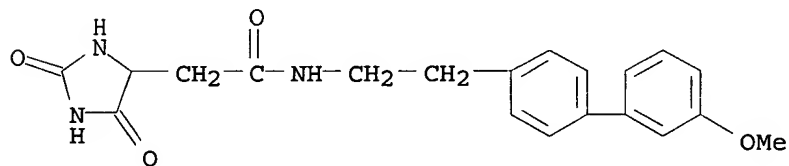
RN 669013-83-6 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(2-benzofuranyl)phenyl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



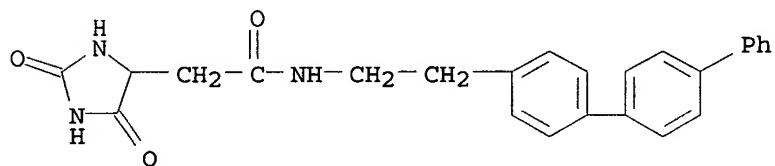
RN 669013-84-7 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3'-methoxy[1,1'-biphenyl]-4-yl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



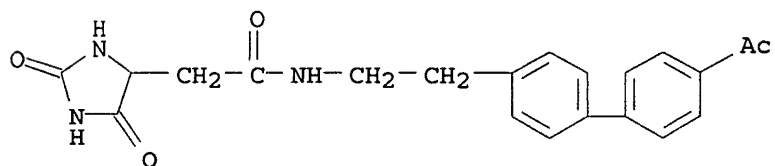
RN 669013-85-8 CAPLUS

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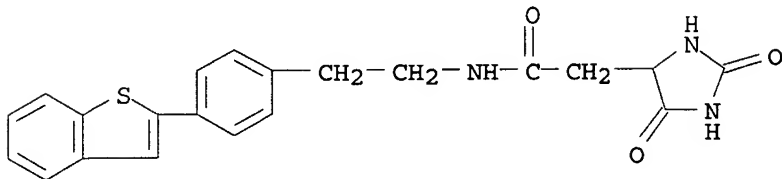
RN 669013-86-9 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-acetyl[1,1'-biphenyl]-4-yl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



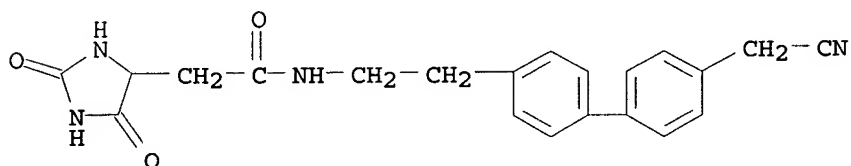
RN 669013-87-0 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4-benzo[b]thien-2-ylphenyl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



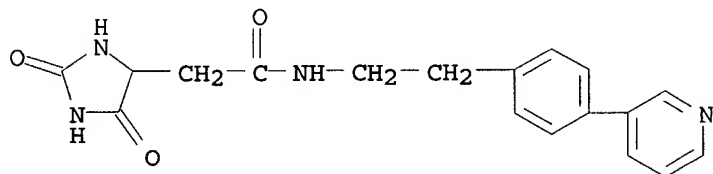
RN 669013-88-1 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4'-(cyanomethyl)[1,1'-biphenyl]-4-yl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



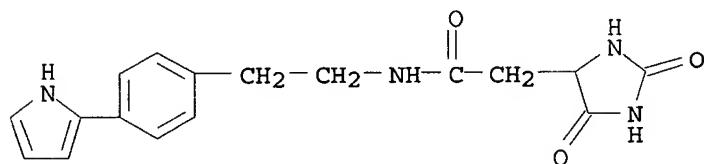
RN 669013-89-2 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4-(3-pyridinyl)phenyl]ethyl]- (9CI) (CA INDEX NAME)



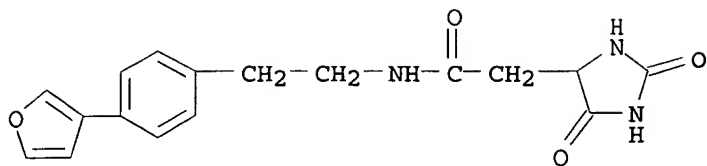
RN 669013-90-5 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4-(1H-pyrrol-2-yl)phenyl]ethyl]- (9CI) (CA INDEX NAME)

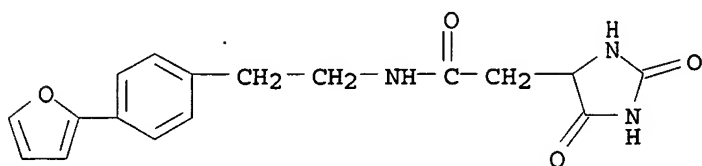


RN 669013-91-6 CAPLUS

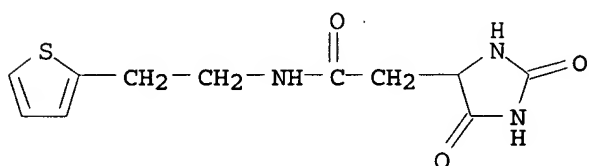
CN 4-Imidazolidineacetamide, N-[2-[4-(3-furanyl)phenyl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



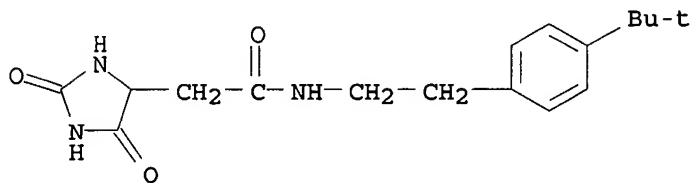
RN 669013-92-7 CAPLUS  
CN 4-Imidazolidineacetamide, N-[2-[4-(2-furanyl)phenyl]ethyl]-2,5-dioxo-  
(9CI) (CA INDEX NAME)



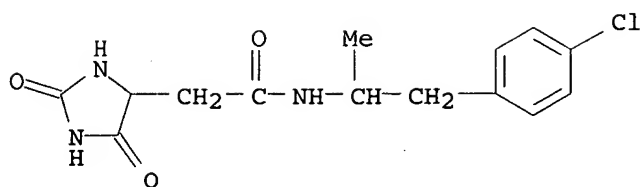
RN 669013-93-8 CAPLUS  
CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-(2-thienyl)ethyl]- (9CI) (CA  
INDEX NAME)



RN 669013-94-9 CAPLUS  
CN 4-Imidazolidineacetamide, N-[2-[4-(1,1-dimethylethyl)phenyl]ethyl]-2,5-  
dioxo- (9CI) (CA INDEX NAME)

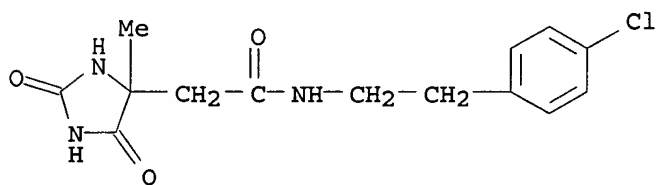


RN 669013-95-0 CAPLUS  
CN 4-Imidazolidineacetamide, N-[2-(4-chlorophenyl)-1-methylethyl]-2,5-dioxo-  
(9CI) (CA INDEX NAME)



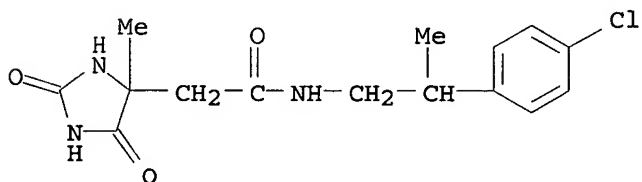
RN 669014-00-0 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4-chlorophenyl)ethyl]-4-methyl-2,5-dioxo-  
(9CI) (CA INDEX NAME)



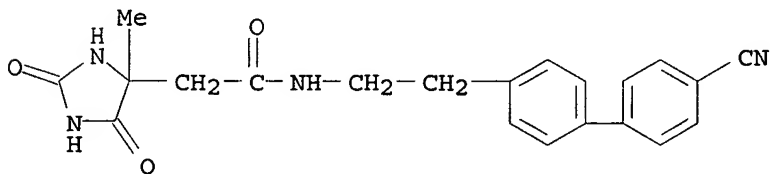
RN 669014-01-1 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4-chlorophenyl)propyl]-4-methyl-2,5-dioxo-  
(9CI) (CA INDEX NAME)



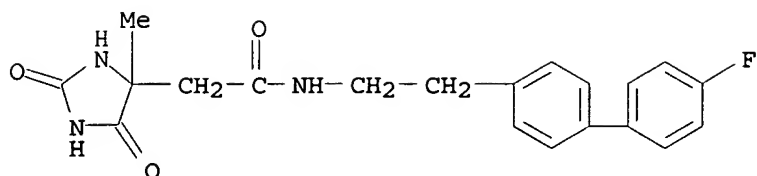
RN 669014-03-3 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-cyano[1,1'-biphenyl]-4-yl)ethyl]-4-methyl-2,5-dioxo-  
(9CI) (CA INDEX NAME)



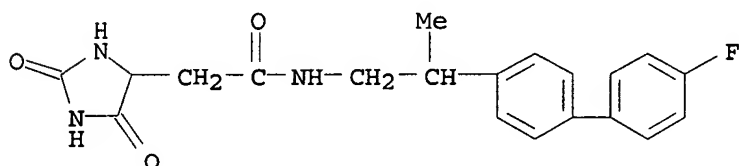
RN 669014-04-4 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-fluoro[1,1'-biphenyl]-4-yl)ethyl]-4-methyl-2,5-dioxo-  
(9CI) (CA INDEX NAME)



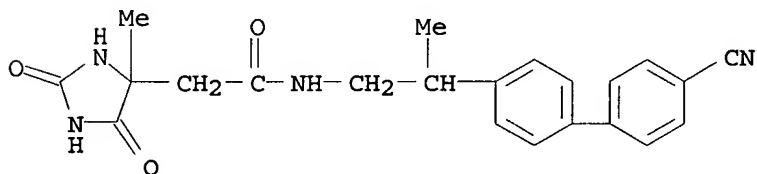
RN 669014-06-6 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-fluoro[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



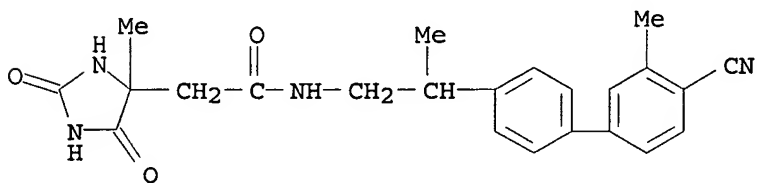
RN 669014-15-7 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-cyano[1,1'-biphenyl]-4-yl)propyl]-4-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)



RN 669014-18-0 CAPLUS

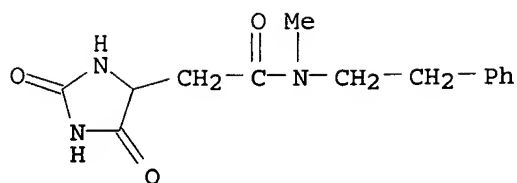
CN 4-Imidazolidineacetamide, N-[2-(4'-cyano-3'-methyl[1,1'-biphenyl]-4-yl)propyl]-4-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)



RN 669014-19-1 CAPLUS

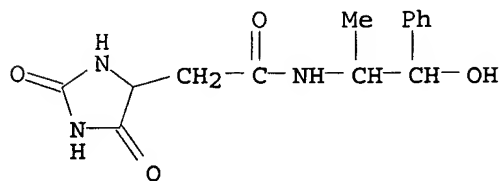
CN 4-Imidazolidineacetamide, N-methyl-2,5-dioxo-N-(2-phenylethyl)- (9CI) (CA INDEX NAME)





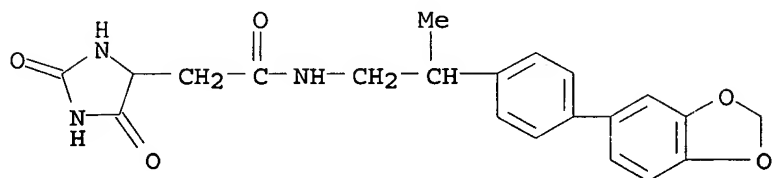
RN 669014-21-5 CAPLUS

CN 4-Imidazolidineacetamide, N-(2-hydroxy-1-methyl-2-phenylethyl)-2,5-dioxo- (9CI) (CA INDEX NAME)



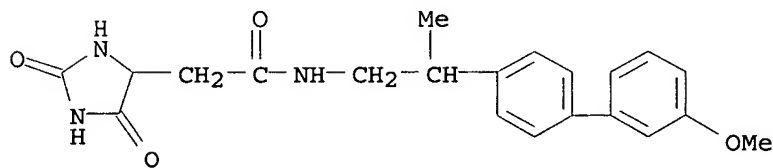
RN 669014-22-6 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(1,3-benzodioxol-5-yl)phenyl]propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



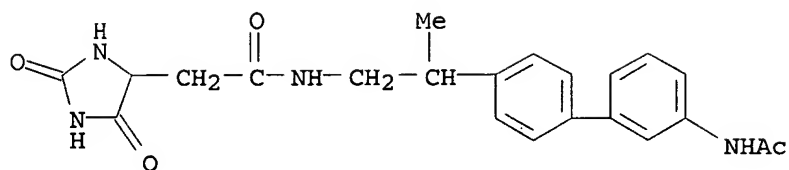
RN 669014-23-7 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3'-methoxy[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



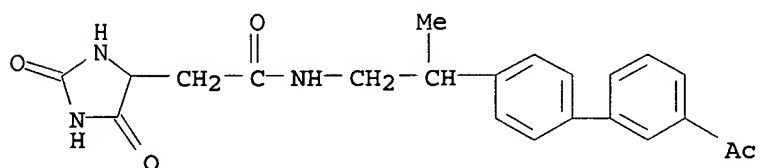
RN 669014-24-8 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[3'-(acetylamino)[1,1'-biphenyl]-4-yl]propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



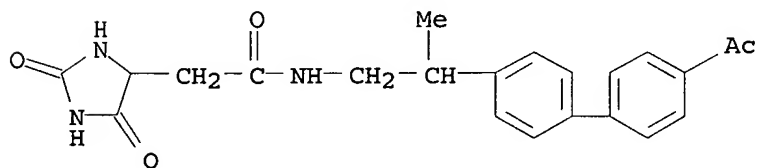
RN 669014-25-9 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3'-acetyl[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



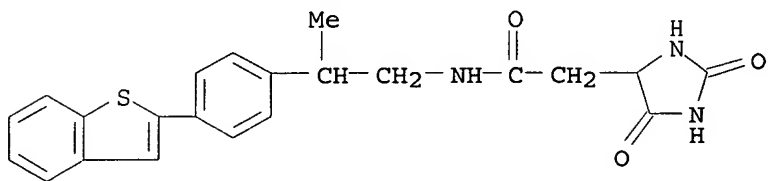
RN 669014-26-0 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-acetyl[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



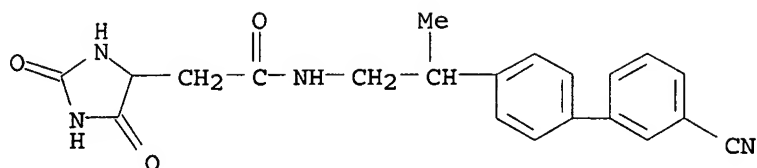
RN 669014-27-1 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4-benzo[b]thien-2-ylphenyl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



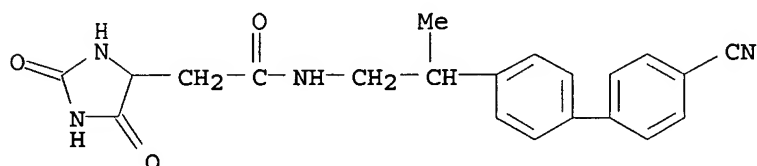
RN 669014-28-2 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3'-cyano[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



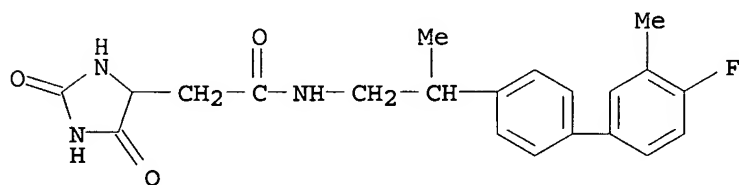
RN 669014-29-3 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-cyano[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



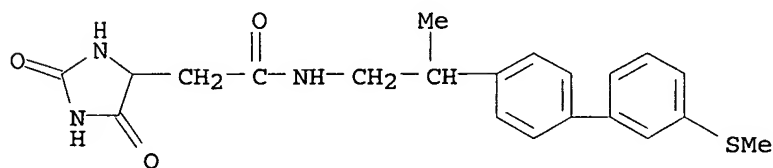
RN 669014-30-6 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-fluoro-3'-methyl[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



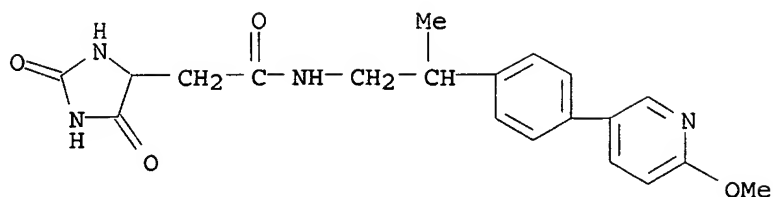
RN 669014-31-7 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[3'-(methylthio)[1,1'-biphenyl]-4-yl]propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



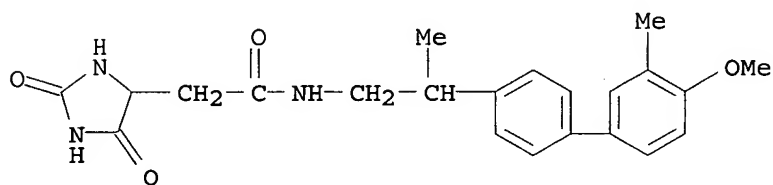
RN 669014-32-8 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(6-methoxy-3-pyridinyl)phenyl]propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



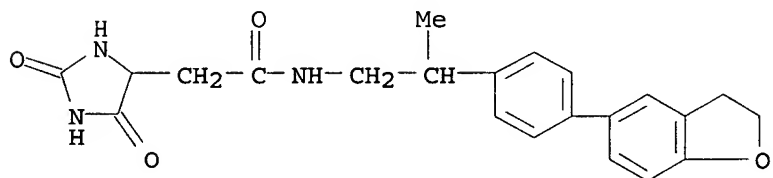
RN 669014-33-9 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-methoxy-3'-methyl[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



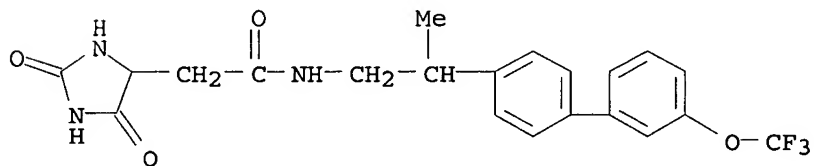
RN 669014-34-0 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(2,3-dihydro-5-benzofuranyl)phenyl]propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



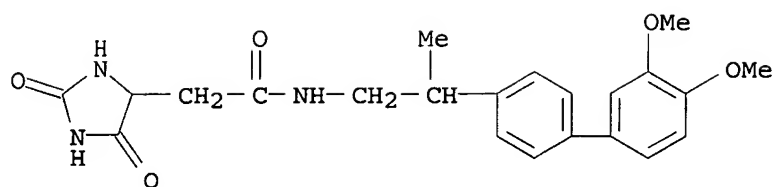
RN 669014-35-1 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]propyl]- (9CI) (CA INDEX NAME)



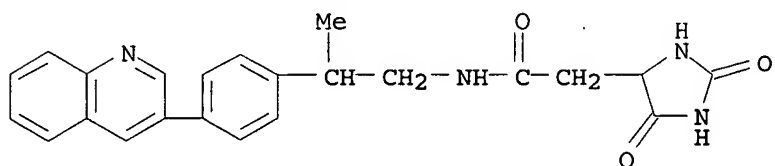
RN 669014-36-2 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3',4'-dimethoxy[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



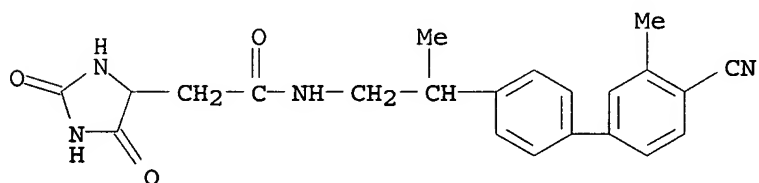
RN 669014-37-3 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4-(3-quinolinyl)phenyl]propyl]- (9CI) (CA INDEX NAME)



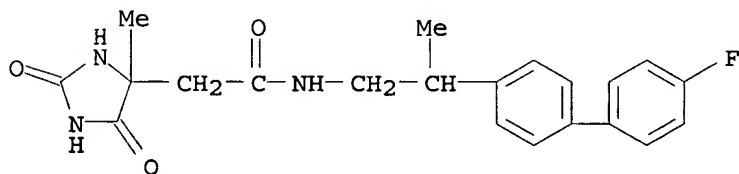
RN 669014-38-4 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-cyano-3'-methyl[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



RN 669014-53-3 CAPLUS

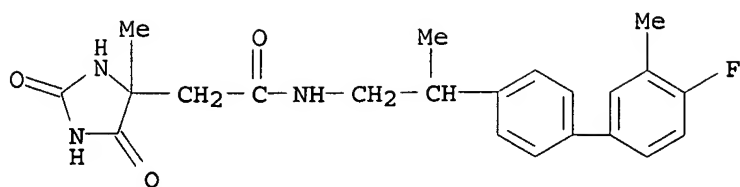
CN 4-Imidazolidineacetamide, N-[2-(4'-fluoro[1,1'-biphenyl]-4-yl)propyl]-4-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)



RN 669014-54-4 CAPLUS

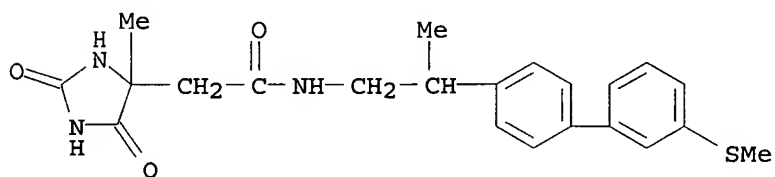
CN 4-Imidazolidineacetamide, N-[2-[4-(1,3-benzodioxol-5-yl)phenyl]propyl]-4-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)





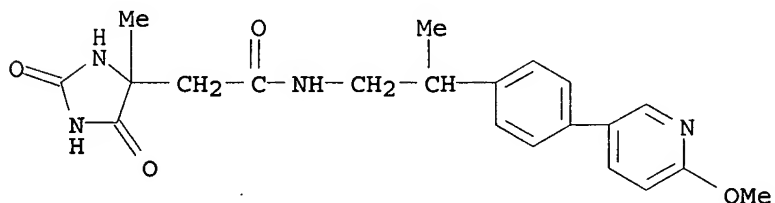
RN 669014-59-9 CAPLUS

CN 4-Imidazolidineacetamide, 4-methyl-N-[2-[3'-(methylthio)[1,1'-biphenyl]-4-yl]propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



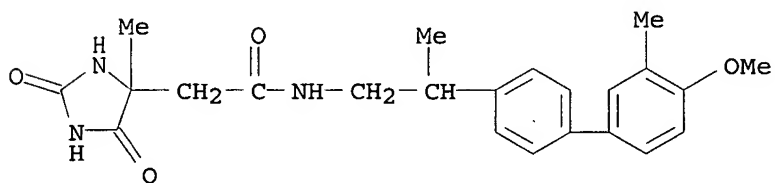
RN 669014-60-2 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(6-methoxy-3-pyridinyl)phenyl]propyl]-4-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)



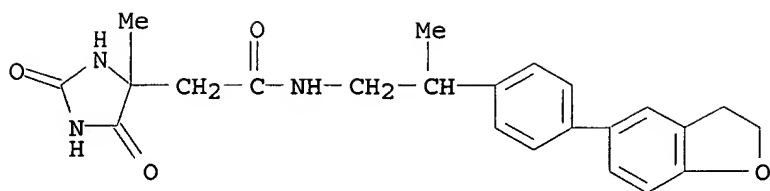
RN 669014-61-3 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-methoxy-3'-methyl[1,1'-biphenyl]-4-yl)propyl]-4-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)



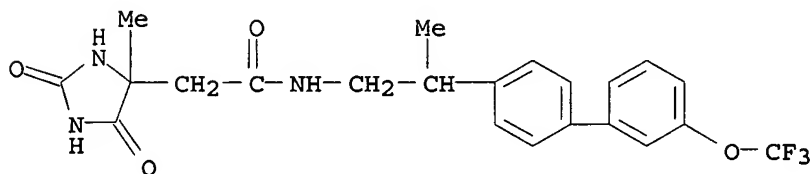
RN 669014-62-4 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(2,3-dihydro-5-benzofuranyl)phenyl]propyl]-4-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)



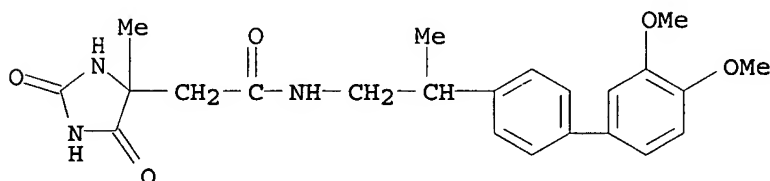
RN 669014-63-5 CAPLUS

CN 4-Imidazolidineacetamide, 4-methyl-2,5-dioxo-N-[2-[3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]propyl]- (9CI) (CA INDEX NAME)



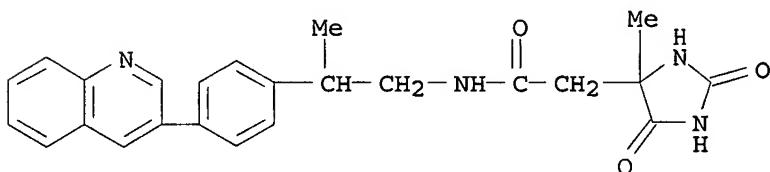
RN 669014-64-6 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3',4'-dimethoxy[1,1'-biphenyl]-4-yl)propyl]-4-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)



RN 669014-65-7 CAPLUS

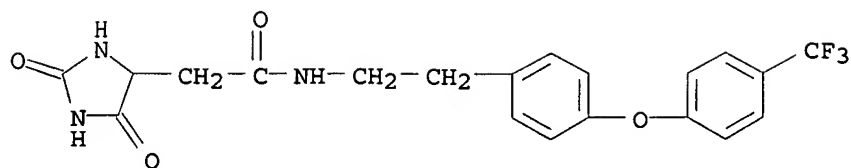
CN 4-Imidazolidineacetamide, 4-methyl-2,5-dioxo-N-[2-[4-(3-quinolinyl)phenyl]propyl]- (9CI) (CA INDEX NAME)



RN 669014-83-9 CAPLUS

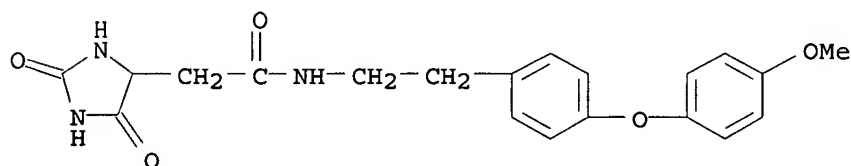
CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4-[4-(trifluoromethyl)phenoxy]phenyl]ethyl]- (9CI) (CA INDEX NAME)





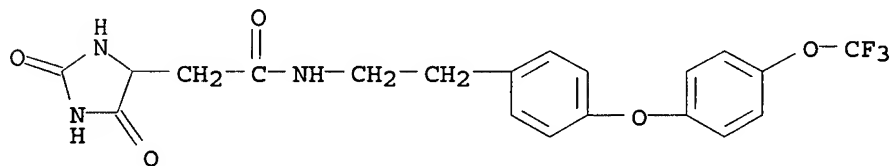
RN 669014-84-0 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(4-methoxyphenoxy)phenyl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



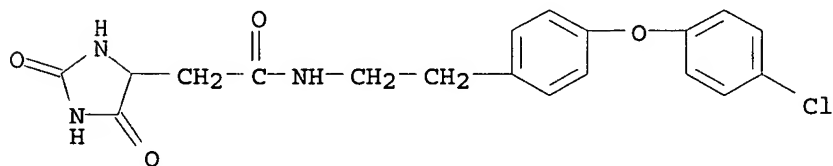
RN 669014-85-1 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4-[4-(trifluoromethoxy)phenoxy]phenyl]ethyl]- (9CI) (CA INDEX NAME)



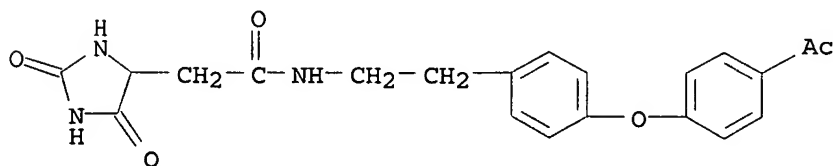
RN 669014-86-2 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(4-chlorophenoxy)phenyl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



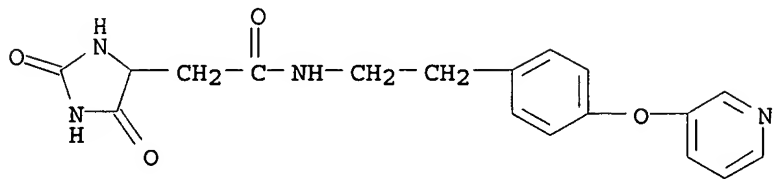
RN 669014-87-3 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(4-acetylphenoxy)phenyl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



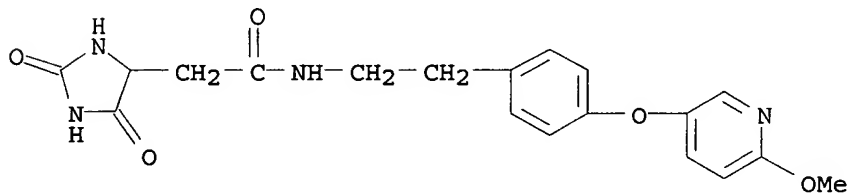
RN 669014-88-4 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4-(3-pyridinyloxy)phenyl]ethyl]-(9CI) (CA INDEX NAME)



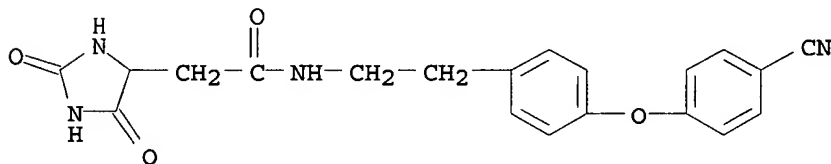
RN 669014-89-5 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-[(6-methoxy-3-pyridinyl)oxy]phenyl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



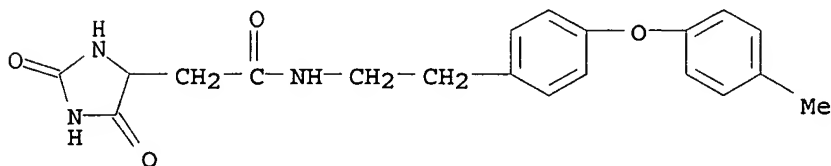
RN 669014-90-8 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(4-cyanophenoxy)phenyl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



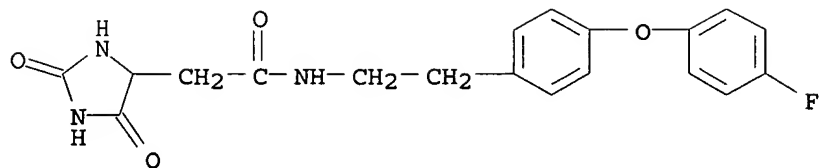
RN 669014-91-9 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(4-methylphenoxy)phenyl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



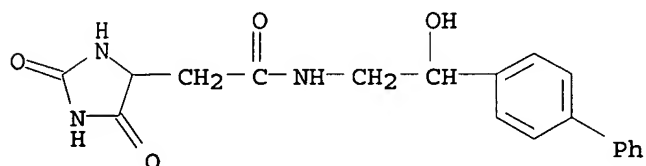
RN 669014-92-0 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(4-fluorophenoxy)phenyl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



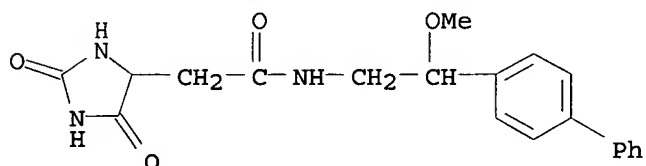
RN 669014-93-1 CAPLUS

CN 4-Imidazolidineacetamide, N-(2-[1,1'-biphenyl]-4-yl-2-hydroxyethyl)-2,5-dioxo- (9CI) (CA INDEX NAME)



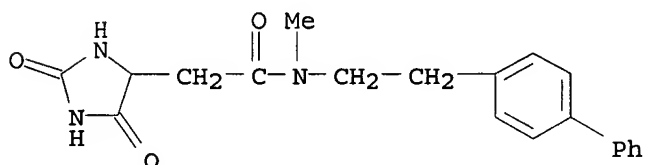
RN 669014-94-2 CAPLUS

CN 4-Imidazolidineacetamide, N-(2-[1,1'-biphenyl]-4-yl-2-methoxyethyl)-2,5-dioxo- (9CI) (CA INDEX NAME)



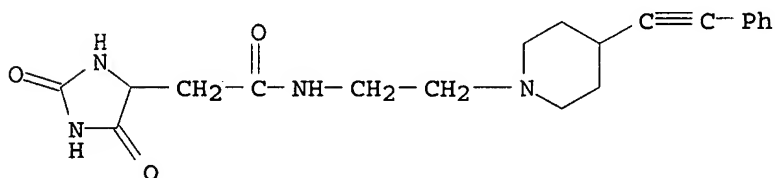
RN 669014-95-3 CAPLUS

CN 4-Imidazolidineacetamide, N-(2-[1,1'-biphenyl]-4-ylethyl)-N-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)



RN 669014-96-4 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4-(phenylethynyl)-1-piperidinyl]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:376819 CAPLUS

DOCUMENT NUMBER: 138:385173

TITLE: Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease

INVENTOR(S): Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy

PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company

SOURCE: PCT Int. Appl., 1243 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

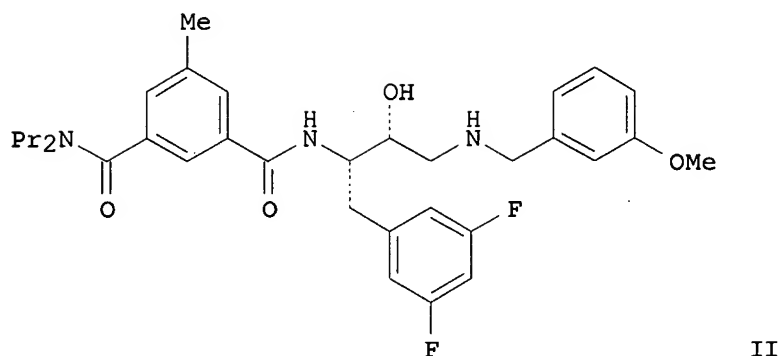
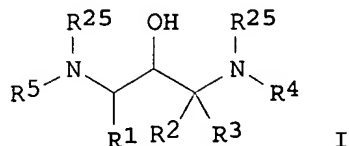
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040096	A2	20030515	WO 2002-US36072	20021108
WO 2003040096	A3	20040506		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2466284	AA	20030515	CA 2002-2466284	20021108
WO 2003040096	A2	20030515	WO 2002-XA36072	20021108
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004171881	A1	20040902	US 2002-291318	20021108
EP 1453789	A2	20040908	EP 2002-793909	20021108
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
BR 2002014035	A	20050426	BR 2002-14035	20021108
JP 2005520791	T2	20050714	JP 2003-542142	20021108
CN 1759095	A	20060412	CN 2002-826786	20021108
ZA 2004003578	A	20051010	ZA 2004-3578	20040511
NO 2004002359	A	20040806	NO 2004-2359	20040607
PRIORITY APPLN. INFO.:			US 2001-337122P	P 20011108
			US 2001-344086P	P 20011228
			US 2002-345635P	P 20020103
			WO 2002-US36072	W 20021108

OTHER SOURCE(S) :  
GI

MARPAT 138:385173



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO<sub>2</sub>, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO<sub>2</sub>, (un)substituted CH<sub>2</sub>; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of  $\beta$ -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC<sub>50</sub> of < 20  $\mu$ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 1 of 1-2 series.

IT 527735-74-6P

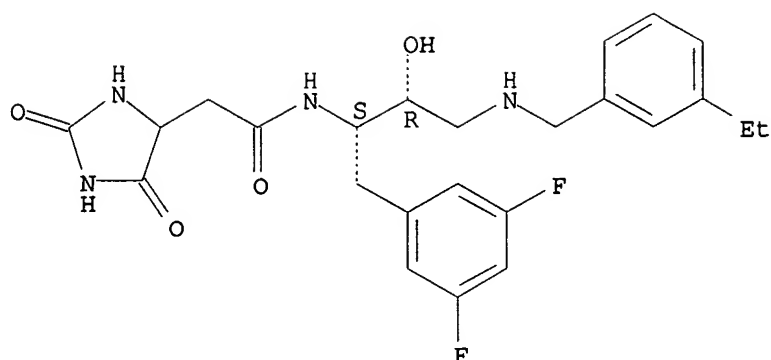
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

RN 527735-74-6 CAPLUS

CN 4-Imidazolidineacetamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-2,5-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:150554 CAPLUS

DOCUMENT NUMBER: 138:188073

TITLE: Preparation of dipeptide heterocyclic aromatic compounds as growth hormone secretagogues

INVENTOR(S): Tino, Joseph A.

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: U.S., 157 pp., Cont.-in-part of U.S. Ser. No. 506,749, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

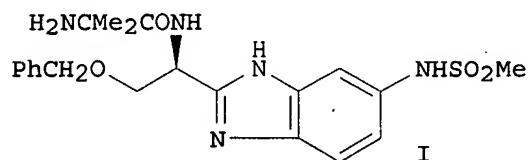
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6525203	B1	20030225	US 2000-662448	20000914
US 6518292	B1	20030211	US 2000-506749	20000218
ZA 2001006854	A	20021120	ZA 2001-6854	20010820
US 6660760	B1	20031209	US 2002-282182	20021028
US 2004002525	A1	20040101	US 2002-281818	20021028
US 6969727	B2	20051129		
US 2004029935	A1	20040212	US 2002-281649	20021028
US 6908938	B2	20050621		
US 2004072881	A1	20040415	US 2002-281848	20021028
PRIORITY APPLN. INFO.:			US 1999-124131P	P 19990312
			US 1999-154919P	P 19990921
			US 2000-506749	A2 20000218

OTHER SOURCE(S): MARPAT 138:188073

GI



AB R1R1aCXaNR6COYXb [R1 = (un)substituted alkyl, (hetero)aryl(alkyl), etc.;

10525640ra.trn

R1a = H or (cyclo)alkyl; R6 = H, (cyclo)alkyl, alkenyl, aryl; Xa = substituted 2-benzoxazolyl, 2-benzothiazolyl, or 2-benzimidazolyl; Xb = (di)(alkyl)amino, (un)substituted imidazolyl; Y = phenylene, (phenylene-interrupted)alkylene, (un)substituted alkylene, aza- or oxaalkylene, or alkenylene] were prepared as growth hormone production and/or release stimulants. Thus, dipeptide benzimidazole derivative I (Boc = tert-butoxycarbonyl) was prepared by a multistep procedure starting from Boc-D-Ser(CH<sub>2</sub>Ph)-OH, 4-nitro-o-phenylenediamine, Boc-methylalanine, and MeSO<sub>2</sub>Cl.

IT 295333-78-7P 295334-02-0P

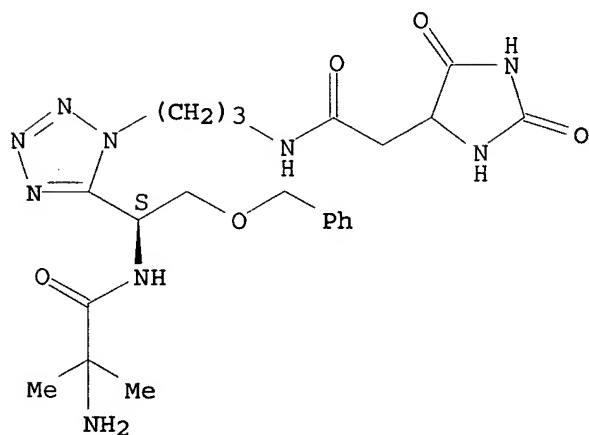
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of dipeptide heterocyclic aromatic compds. as growth hormone secretagogues)

RN 295333-78-7 CAPLUS

CN 4-Imidazolidineacetamide, N-[3-[5-[(1S)-1-[(2-amino-2-methyl-1-oxopropyl)amino]-2-(phenylmethoxy)ethyl]-1H-tetrazol-1-yl]propyl]-2,5-dioxo-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

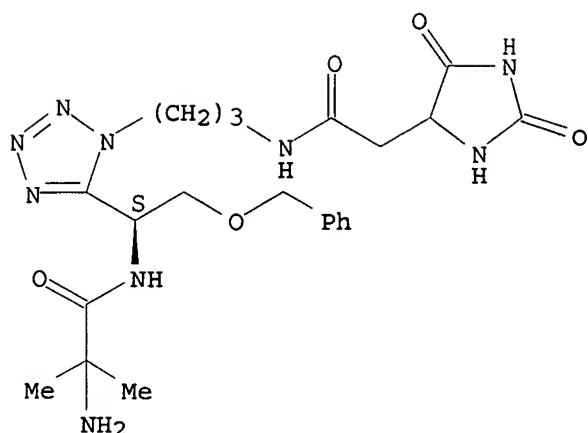


● HCl

RN 295334-02-0 CAPLUS

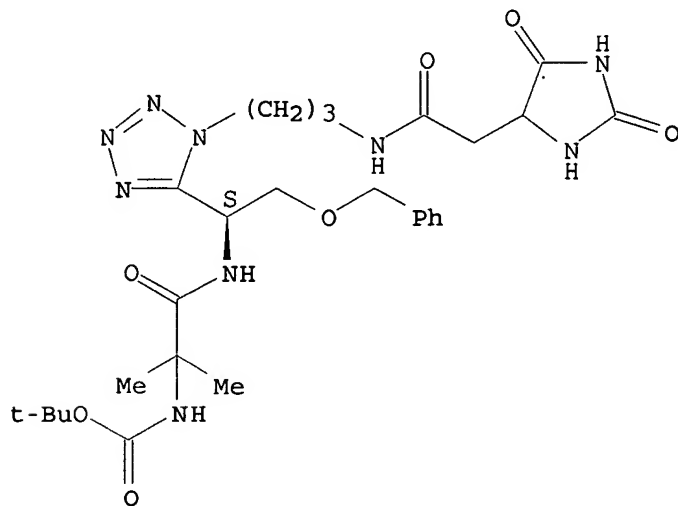
CN 4-Imidazolidineacetamide, N-[3-[5-[(1S)-1-[(2-amino-2-methyl-1-oxopropyl)amino]-2-(phenylmethoxy)ethyl]-1H-tetrazol-1-yl]propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 295338-27-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of dipeptide heterocyclic aromatic compds. as growth hormone  
 secretagogues)  
 RN 295338-27-1 CAPLUS  
 CN Carbamic acid, [2-[[[(1S)-1-[1-[3-[[2,5-dioxo-4-  
 imidazolidinyl) acetyl] amino] propyl]-1H-tetrazol-5-yl]-2-  
 (phenylmethoxy) ethyl] amino]-1,1-dimethyl-2-oxoethyl]-, 1,1-dimethylethyl  
 ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



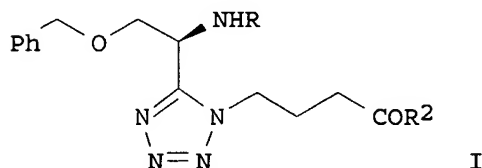
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2000:666562 CAPLUS  
 DOCUMENT NUMBER: 133:252748  
 TITLE: Preparation of methylalanyl-O-benzyltyrosine  
 derivatives as growth hormone production and/or  
 release stimulants



INVENTOR(S): Robl, Jeffrey; Tino, Joseph A.; Hernandez, Andres S.;  
 Li, James J.; Li, Jun; Swartz, Stephen G.  
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
 SOURCE: PCT Int. Appl., 205 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000054729	A2	20000921	WO 2000-US5704	20000302
WO 2000054729	A3	20010111		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2367461	AA	20000921	CA 2000-2367461	20000302
EP 1175213	A2	20020130	EP 2000-913733	20000302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200102780	T2	20020821	TR 2001-200102780	20000302
BR 2000008937	A	20020924	BR 2000-8937	20000302
JP 2002539141	T2	20021119	JP 2000-604808	20000302
EE 200100479	A	20021216	EE 2001-479	20000302
ZA 2001006854	A	20021120	ZA 2001-6854	20010820
BG 105843	A	20020531	BG 2001-105843	20010824
LT 4958	B	20021025	LT 2001-87	20010824
LV 12752	B	20031020	LV 2001-132	20010906
NO 2001004407	A	20011108	NO 2001-4407	20010911
PRIORITY APPLN. INFO.:			US 1999-124131P	P 19990312
			US 1999-154919P	P 19990921
			WO 2000-US5704	W 20000302
OTHER SOURCE(S):		MARPAT 133:252748		
GI				



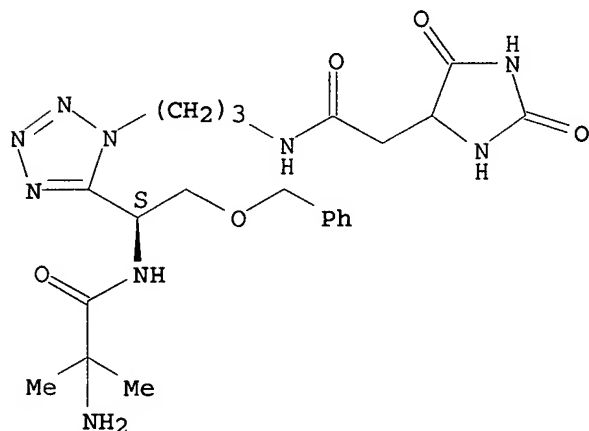
AB R1R1aCXaNR6COYXb [R1 = (un)substituted alkyl, (hetero)aryl(alkyl), etc.; R1a = H or (cyclo)alkyl; R6 = H, (cyclo)alkyl, alkenyl, aryl; Xa = (un)substituted heteroaryl; Xb = (di)(alkyl)amino, (un)substituted imidazolyl, etc.; Y = phenylene, (phenylene-interrupted)alkylene, alkenylene, etc.] were prepared as growth hormone production and/or release stimulants (no data). Thus, (R)-PhCH2OCH2CH(NHCO2CMe3)CO2H was amidated by H2N(CH2)3CO2Me and the product cyclocondensed with Me3SiN3 to give, after deprotection, O-benzyltyrosine derivative I (R = H, R2 = OMe) which was amidated by BocNHCMMe2CO2H to give, in 3 addnl. steps, I.CF3CO2H (R =

COCMe<sub>2</sub>NH<sub>2</sub>, R<sub>2</sub> = NHCH<sub>2</sub>CH<sub>2</sub>R<sub>3</sub>, R<sub>3</sub> = 3-indolyl).

IT 295333-78-7P 295334-02-0P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of methylalanyl-O-benzyltyrosine derivs. as growth hormone production and/or release stimulants)

RN 295333-78-7 CAPLUS  
 CN 4-Imidazolidineacetamide, N-[3-[5-[(1S)-1-[(2-amino-2-methyl-1-oxopropyl)amino]-2-(phenylmethoxy)ethyl]-1H-tetrazol-1-yl]propyl]-2,5-dioxo-, monohydrochloride (9CI) (CA INDEX NAME)

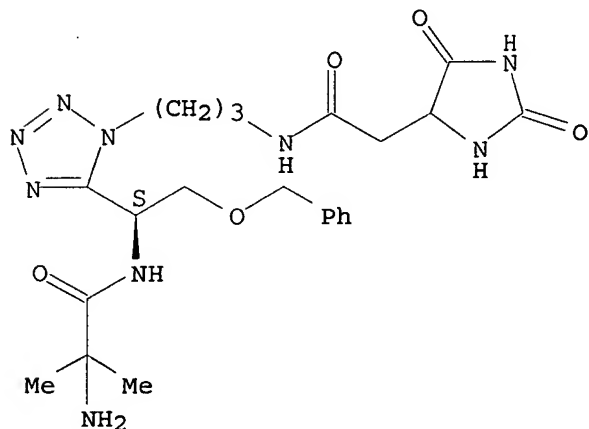
Absolute stereochemistry.



● HCl

RN 295334-02-0 CAPLUS  
 CN 4-Imidazolidineacetamide, N-[3-[5-[(1S)-1-[(2-amino-2-methyl-1-oxopropyl)amino]-2-(phenylmethoxy)ethyl]-1H-tetrazol-1-yl]propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 295338-27-1P

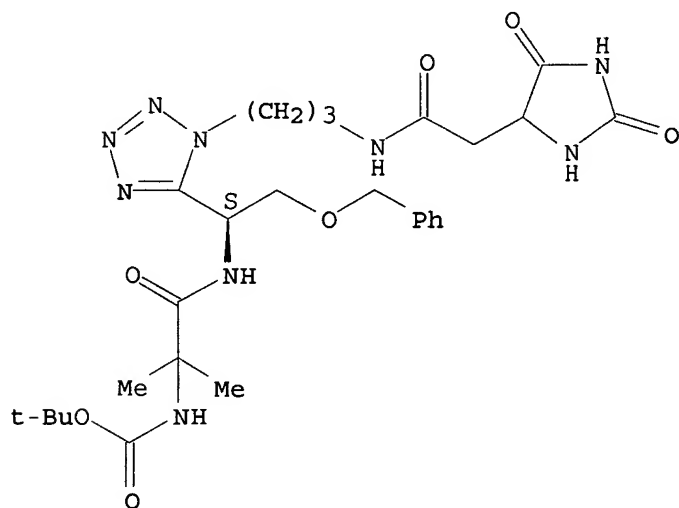
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of methylalanyl-O-benzyltyrosine derivs. as growth hormone production and/or release stimulants)

RN 295338-27-1 CAPLUS

CN Carbamic acid, [2-[[[(1S)-1-[1-[3-[[[(2,5-dioxo-4-imidazolidinyl)acetyl]amino]propyl]-1H-tetrazol-5-yl]-2-(phenylmethoxy)ethyl]amino]-1,1-dimethyl-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:388199 CAPLUS

DOCUMENT NUMBER: 125:58489

TITLE: Preparation of N-acylated 2-heterocycloethylamines as nonpeptide antagonists of SP and NKA

INVENTOR(S): Russell, Keith

PATENT ASSIGNEE(S): Zeneca Limited, UK; Astrazeneca AB

SOURCE: Eur. Pat. Appl., 40 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 709375	A2	19960501	EP 1995-307496	19951020
EP 709375	A3	19980826		
EP 709375	B1	20050518		
R: CH, DE, ES, FR, GB, IT, LI				
JP 08208605	A2	19960813	JP 1995-275847	19951024
US 5710169	A	19980120	US 1995-547512	19951024
US 5998444	A	19991207	US 1997-979995	19971126
US 6147083	A	20001114	US 1999-384444	19990827
PRIORITY APPLN. INFO.:			GB 1994-21411	A 19941025
			GB 1995-12367	A 19950617

US 1995-547512

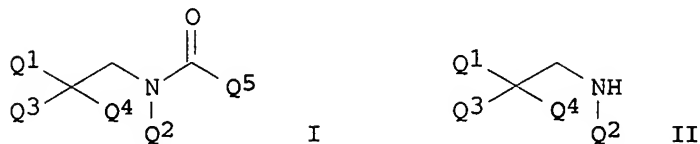
A3 19951024

US 1997-979995

A3 19971126

OTHER SOURCE(S):  
GI

CASREACT 125:58489; MARPAT 125:58489



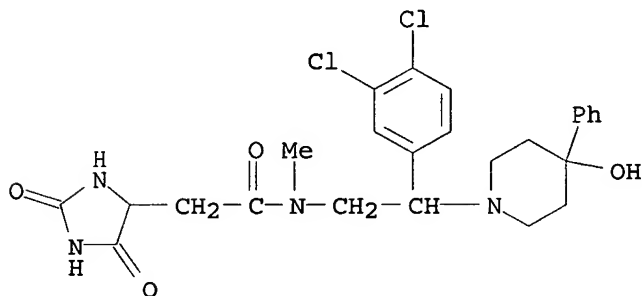
AB The title compds. [I; Q1 = (substituted) piperidino, piperazino, pyrrolidino, etc.; Q2, Q3 = H, C1-3 alkyl; Q4 = (substituted) Ph, thienyl, imidazolyl, etc.; Q5 = (substituted) C1-8 alkyl, aryl, formyl, etc.] and its salts, useful for the treatment of asthma, were prepared by acylation of amine II with the corresponding acid or acid chloride. Thus, acylation of the piperidinoethylamine II [Q1 = 4-hydroxy-4-phenylpiperidino; Q2 = Me; Q3 = H; Q4 = 3,4-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>] with 2-MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>COOH in the presence of 1,1'-carbonyldiimidazole in THF followed by treatment with HCl afforded I.HCl [Q5 = 2-MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>]. In general, compds. I showed K<sub>i</sub> of ≤ 1 μM against SP receptor binding and K<sub>i</sub> ≤ 10 μM against neurokinin A (NKA) receptor binding.

IT 178166-64-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of N-acylated 2-heterocycloethylamines as nonpeptide antagonists of SP and NKA)

RN 178166-64-8 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3,4-dichlorophenyl)-2-(4-hydroxy-4-phenyl-1-piperidiny)ethyl]-N-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)



=&gt; log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

44.57

451.68

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-6.00

-15.75

Page 60

STN INTERNATIONAL LOGOFF AT 09:59:49 ON 19 APR 2006

10525640ra.trn

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAJRK1626

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 "Ask CAS" for self-help around the clock  
NEWS 3 DEC 23 New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/  
USPAT2  
NEWS 4 JAN 13 IPC 8 searching in IFIPAT, IFIUDB, and IFICDB  
NEWS 5 JAN 13 New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to  
INPADOC  
NEWS 6 JAN 17 Pre-1988 INPI data added to MARPAT  
NEWS 7 JAN 17 IPC 8 in the WPI family of databases including WPIFV  
NEWS 8 JAN 30 Saved answer limit increased  
NEWS 9 FEB 21 STN AnaVist, Version 1.1, lets you share your STN AnaVist  
visualization results  
NEWS 10 FEB 22 The IPC thesaurus added to additional patent databases on STN  
NEWS 11 FEB 22 Updates in EPFULL; IPC 8 enhancements added  
NEWS 12 FEB 27 New STN AnaVist pricing effective March 1, 2006  
NEWS 13 FEB 28 MEDLINE/LMEDLINE reload improves functionality  
NEWS 14 FEB 28 TOXCENTER reloaded with enhancements  
NEWS 15 FEB 28 REGISTRY/ZREGISTRY enhanced with more experimental spectral  
property data  
NEWS 16 MAR 01 INSPEC reloaded and enhanced  
NEWS 17 MAR 03 Updates in PATDPA; addition of IPC 8 data without attributes  
NEWS 18 MAR 08 X.25 communication option no longer available after June 2006  
NEWS 19 MAR 22 EMBASE is now updated on a daily basis  
NEWS 20 APR 03 New IPC 8 fields and IPC thesaurus added to PATDPAFULL  
NEWS 21 APR 03 Bibliographic data updates resume; new IPC 8 fields and IPC  
thesaurus added in PCTFULL  
NEWS 22 APR 04 STN AnaVist \$500 visualization usage credit offered  
NEWS 23 APR 12 LINSPEC, learning database for INSPEC, reloaded and enhanced  
NEWS 24 APR 12 Improved structure highlighting in FQHIT and QHIT display  
in MARPAT  
NEWS 25 APR 12 Derwent World Patents Index to be reloaded and enhanced during  
second quarter; strategies may be affected  
  
NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,  
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.  
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT  
<http://download.cas.org/express/v8.0-Discover/>  
  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS LOGIN Welcome Banner and News Items  
NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that

specific topic.

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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 17:57:39 ON 18 APR 2006

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 17:57:47 ON 18 APR 2006

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STRUCTURE FILE UPDATES: 17 APR 2006 HIGHEST RN 880759-42-2  
DICTIONARY FILE UPDATES: 17 APR 2006 HIGHEST RN 880759-42-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

\*\*\*\*\*  
\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

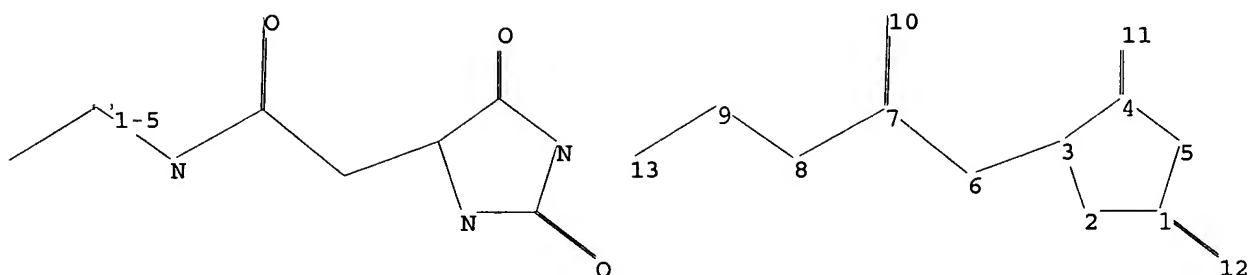
Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10525640\Struc 3.str



```

chain nodes :
6 7 8 9 10 11 12 13
ring nodes :
1 2 3 4 5
chain bonds :
1-12 3-6 4-11 6-7 7-8 7-10 8-9 9-13
ring bonds :
1-2 1-5 2-3 3-4 4-5
exact/norm bonds :
1-2 1-5 1-12 2-3 3-4 4-5 4-11 7-8 7-10 8-9
exact bonds :
3-6 6-7 9-13

```

```

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS
10:CLASS 11:CLASS 12:CLASS 13:CLASS

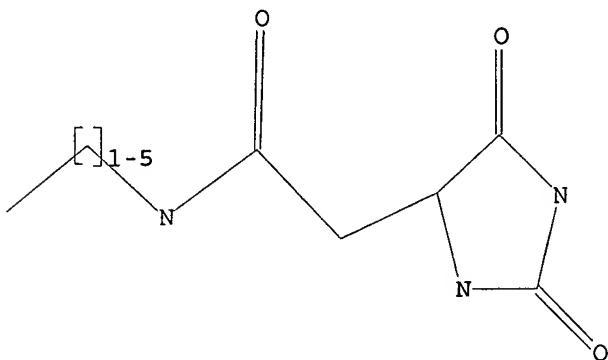
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L1 STRUCTURE UPLOADED

```

=> d
L1 HAS NO ANSWERS
L1 STR

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Structure attributes must be viewed using STN Express query preparation.

=> l1

10525640.trn



Page 4

SAMPLE SEARCH INITIATED 17:58:00 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS 6 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 9 TO 360  
PROJECTED ANSWERS: 6 TO 266

L2 6 SEA SSS SAM L1

=> l1 full  
FULL SEARCH INITIATED 17:58:04 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 220 TO ITERATE

100.0% PROCESSED 220 ITERATIONS 143 ANSWERS  
SEARCH TIME: 00.00.01

L3 143 SEA SSS FUL L1

=> file medline caplus  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
ENTRY SESSION  
FULL ESTIMATED COST 166.94 167.15

FILE 'MEDLINE' ENTERED AT 17:58:10 ON 18 APR 2006

FILE 'CAPLUS' ENTERED AT 17:58:10 ON 18 APR 2006  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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=> l3  
L4 37 L3

=> file reg  
COST IN U.S. DOLLARS SINCE FILE TOTAL  
ENTRY SESSION  
FULL ESTIMATED COST 6.26 173.41

FILE 'REGISTRY' ENTERED AT 18:02:27 ON 18 APR 2006  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 17 APR 2006 HIGHEST RN 880759-42-2  
DICTIONARY FILE UPDATES: 17 APR 2006 HIGHEST RN 880759-42-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

10525640.trn

```
*****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005. A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*
*****
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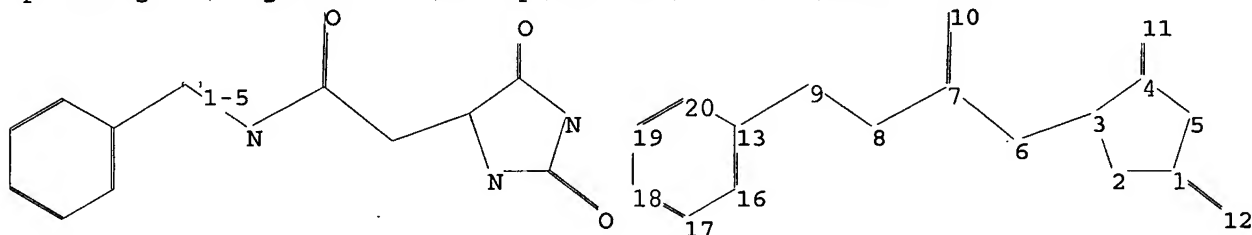
Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10525640\Struc 4.str



chain nodes :

6 7 8 9 10 11 12

ring nodes :

1 2 3 4 5 13 16 17 18 19 20

chain bonds :

1-12 3-6 4-11 6-7 7-8 7-10 8-9 9-13

ring bonds :

1-2 1-5 2-3 3-4 4-5 13-16 13-20 16-17 17-18 18-19 19-20

exact/norm bonds :

1-2 1-5 1-12 2-3 3-4 4-5 4-11 7-8 7-10 8-9

exact bonds :

3-6 6-7 9-13

normalized bonds :

13-16 13-20 16-17 17-18 18-19 19-20

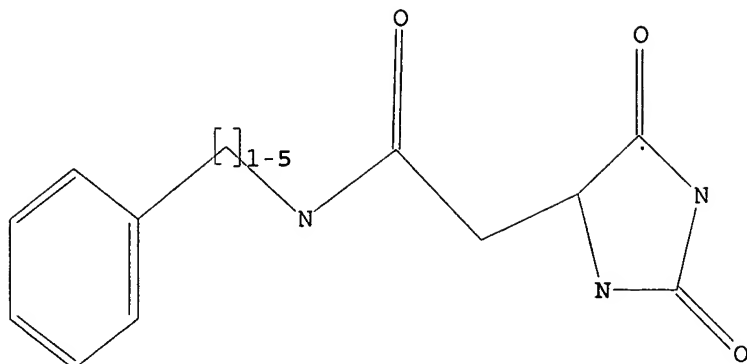
Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:CLASS 9:CLASS  
10:CLASS 11:CLASS 12:CLASS 13:CLASS 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom

L5 STRUCTURE UPLOADED

10525640.trn

=> d  
L5 HAS NO ANSWERS  
L5 STR



Structure attributes must be viewed using STN Express query preparation.

=> 15  
SAMPLE SEARCH INITIATED 18:03:20 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 8 TO ITERATE

100.0% PROCESSED 8 ITERATIONS 2 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 8 TO 329  
PROJECTED ANSWERS: 2 TO 124

L6 2 SEA SSS SAM L5

=> 15 full  
FULL SEARCH INITIATED 18:03:23 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 216 TO ITERATE

100.0% PROCESSED 216 ITERATIONS 98 ANSWERS  
SEARCH TIME: 00.00.01

L7 98 SEA SSS FUL L5

=> file medline caplus  
COST IN U.S. DOLLARS  
FULL ESTIMATED COST  
SINCE FILE ENTRY 167.38  
TOTAL SESSION 340.79

FILE 'MEDLINE' ENTERED AT 18:03:31 ON 18 APR 2006

FILE 'CAPLUS' ENTERED AT 18:03:31 ON 18 APR 2006  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

=> 17  
L8 9 L7

=> dup rem l8  
 PROCESSING COMPLETED FOR L8  
 L9 9 DUP REM L8 (0 DUPLICATES REMOVED)

=> d ibib abs hitstr 1-9

L9 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2005:1021606 CAPLUS  
 DOCUMENT NUMBER: 143:326096  
 TITLE: Preparation of substituted urea and carbamate,  
 phenacyl-2-hydroxy-3-diaminoalkane, and  
 benzamide-2-hydroxy-3-diaminoalkane aspartyl protease  
 and  $\beta$ -secretase inhibitors for treating  
 conditions associated with amyloidosis such as  
 Alzheimer's disease  
 INVENTOR(S): John, Varghese; Maillard, Michel; Tucker, John;  
 Aquino, Jose; Hom, Roy; Tung, Jay; Dressen, Darren;  
 Shah, Neerav; Neitz, R. Jeffrey  
 PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 532 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005087215	A1	20050922	WO 2005-US7775	20050309
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005261273	A1	20051124	US 2005-75292	20050309
PRIORITY APPLN. INFO.:			US 2004-551192P	P 20040309
			US 2004-575829P	P 20040602
			US 2004-591857P	P 20040729
			US 2004-622589P	P 20041028

OTHER SOURCE(S): MARPAT 143:326096

AB The invention is related to compds. of formula  $R_2NHCH(R_1)CH(OH)CH_2NHR_c$  (I)  
 [R1 = (un)substituted benzyl, thien-2-ylmethyl, etc.; R2 = NH2 and  
 derivs., SO2-aryl, hetero/aryl-U, etc.; U = CO, CS, CONH and derivs.,  
 etc.; Rc = carbocyclyl or heterocyclyl; with addnl. details given in the  
 claims] particularly acetyl 2-hydroxy-1,3-diaminospirocyclohexanes and  
 derivs., that are useful in treating diseases, disorders, and conditions  
 associated with amyloidosis. Amyloidosis refers to a collection of diseases,  
 disorders, and conditions associated with abnormal deposition of A- $\beta$   
 protein. For example, alkylation of (2R,3S)-3-amino-1-[[1-(3-tert-  
 butylphenyl)cyclohexyl]amino]-4-(3,5-difluorophenyl)butan-2-ol $\cdot$ 2HCl  
 with 4-iodobenzamide gave the corresponding amide. Selected I displayed  
 IC50 values < 5  $\mu$ M in a cell free inhibition assay utilizing a  
 synthetic APP substrate that can be cleaved by  $\beta$ -secretase. The

selectivity of I for  $\beta$ -secretase vs. cathepsin D for 6 examples of I are tabulated. Brain uptake, total polar surface area and/or lipophilicity for 32 examples of I are tabulated.

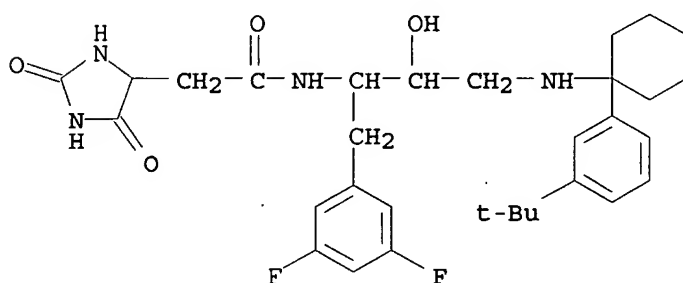
IT 865375-15-1P, N-[3-[[1-(3-tert-Butylphenyl)cyclohexyl]amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-2-(2,5-dioxoimidazolidin-4-yl)acetamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of as aspartyl protease and  $\beta$ -secretase inhibitors)

RN 865375-15-1 CAPLUS

CN 4-Imidazolidineacetamide, N-[1-[(3,5-difluorophenyl)methyl]-3-[[1-[3-(1,1-dimethylethyl)phenyl]cyclohexyl]amino]-2-hydroxypropyl]-2,5-dioxo- (9CI)  
(CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:701970 CAPLUS

DOCUMENT NUMBER: 141:225511

TITLE: Preparation of substituted azoles as protein tyrosine phosphatase inhibitors for treatment of diabetes and other PTPase mediated conditions

INVENTOR(S): Mjalli, Adnan M. M.; Andrews, Robert C.; Yarragunta, Ravindra R.; Xie, Rongyuan; Ren, Tan; Subramanian, Govindan; Quada, James C., Jr.

PATENT ASSIGNEE(S): Transtech Pharma Inc., USA

SOURCE: PCT Int. Appl., 224 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

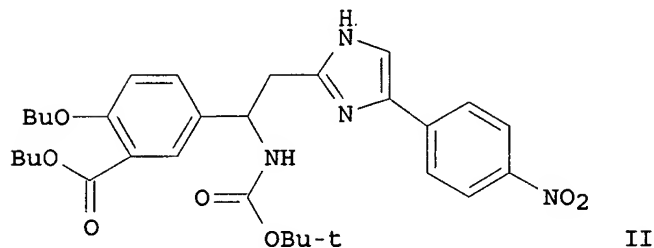
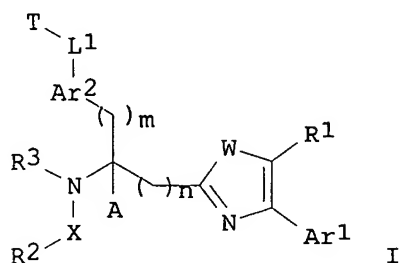
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004071448	A2	20040826	WO 2004-US4076	20040212
WO 2004071448	A3	20041014		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004186151 A1 20040923 US 2004-777471 20040212  
 PRIORITY APPLN. INFO.: US 2003-446924P P 20030212  
 OTHER SOURCE(S): MARPAT 141:225511  
 GI



AB Title imidazoles and analogs I [wherein m, n = independently 0, 1; A = H, alkyl, alkenyl, alkynyl; L1 = a bond, O, alkylene, CO, NHCO, NH, NHSO2, etc.; T = H, (un)substituted (cyclo)alkyl, heterocyclyl, (hetero)aryl, etc.; W = O, S, NR4; X = a bond, CO, CH2, SO2; R1 = H, halo, CN, alkyl, (hetero)aryl, heterocyclyl, etc.; R2 = H, perfluoroalkyl, alkylene optionally interrupted by one or more heteroatoms, (hetero)aryl, heterocyclyl, etc.; R3 = H, alkyl, (cyclo)alkylalkylene, (hetero)aryl(alkylene); R4 = H, alkyl, (hetero)aryl(alkyl), heterocyclyl(alkyl), etc.; Ar1 = (un)substituted optionally fused (hetero)aryl; Ar2 = (un)substituted optionally fused (hetero)arylene; and pharmaceutically acceptable salts, solvates, and prodrugs thereof] were prepared as inhibitors of protein tyrosine phosphatases (PTPases). For example, 3-[(tert-butoxycarbonyl)amino]-2-(4-butoxy-3-butoxycarbonylphenyl)-2-ethyl-4-(4-nitrophenyl)imidazole was coupled with 4-nitrophenacyl bromide to give the keto ester, which was treated with ammonium acetate in glacial acetic acid/anhydrous DMF to afford the imidazole II (40%). Compds. of the invention inhibited PTP 1B activity with IC50 values ranging from about 0.01  $\mu$ M to about 20  $\mu$ M. Thus, I and pharmaceutical compns. comprising them may be useful for the management, treatment, control, and adjunct treatment of diseases mediated by PTPase activity, such as Type I diabetes, Type II diabetes, immune dysfunction, AIDS, autoimmune diseases, glucose intolerance, obesity, cancer, psoriasis, allergic diseases, infectious diseases, inflammatory diseases, diseases involving the modulated synthesis and/or production of growth hormone

or cytokines, of Alzheimer's disease (no data).

IT 745834-40-6P

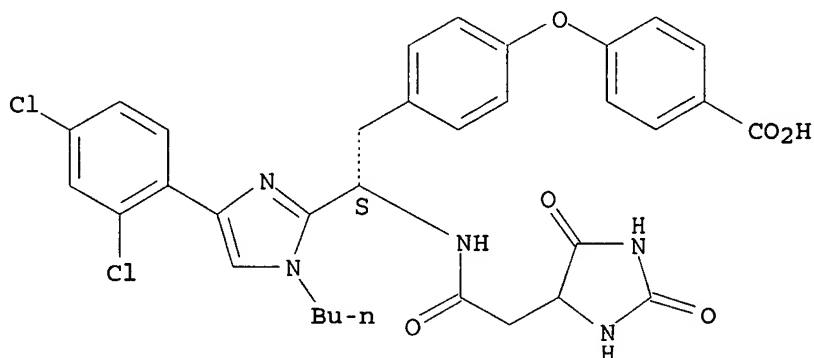
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PTPase inhibitor; preparation of substituted imidazoles as PTPase inhibitors for treatment of diabetes and other PTPase mediated conditions)

RN 745834-40-6 CAPLUS

CN Benzoic acid, 4-[4-[(2S)-2-[1-butyl-4-(2,4-dichlorophenyl)-1H-imidazol-2-yl]-2-[[2,5-dioxo-4-imidazolidinyl)acetyl]amino]ethyl]phenoxy] - (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:203815 CAPLUS

DOCUMENT NUMBER: 140:235715

TITLE: Preparation of 2,5-dioxoimidazolidin-4-yl acetamide derivatives as inhibitors of metalloproteinase MMP12

INVENTOR(S): Henriksson, Krister; Munck Af Rosenschoeld, Magnus

PATENT ASSIGNEE(S): Astrazeneca AB, Swed.

SOURCE: PCT Int. Appl., 87 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

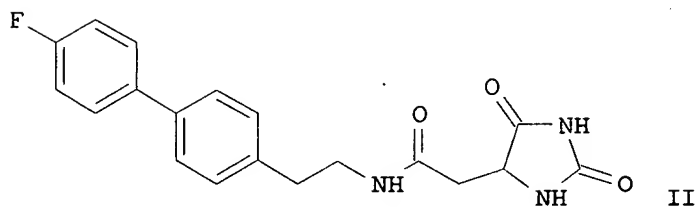
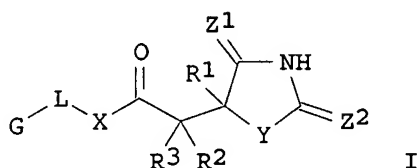
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020415	A1	20040311	WO 2003-SE1328	20030826
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2495853	AA	20040311	CA 2003-2495853	20030826
AU 2003253557	A1	20040319	AU 2003-253557	20030826

BR 2003013635	A	20050621	BR 2003-13635	20030826
EP 1542977	A1	20050622	EP 2003-791528	20030826
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006503019	T2	20060126	JP 2004-532506	20030826
US 2005245586	A1	20051103	US 2005-525640	20050225
NO 2005001540	A	20050323	NO 2005-1540	20050323
PRIORITY APPLN. INFO.:			SE 2002-2539	A 20020827
			WO 2003-SE1328	W 20030826
OTHER SOURCE(S):			CASREACT 140:235715; MARPAT 140:235715	
GI				



AB The title compound I [X= O, CH<sub>2</sub>, or (substituted)amino; Y = NH or N-Me; Z<sub>1</sub>, Z<sub>2</sub> = each represent an oxygen or sulfur atom, with the proviso that at least one of Z<sub>1</sub>, Z<sub>2</sub> represents an oxygen atom; R<sub>1</sub> = H, alkyl, (un)saturated 3-10 membered ring system which may comprise at least one ring heteroatom selected from nitrogen, oxygen and sulfur, etc.; R<sub>2</sub>, R<sub>3</sub> = H or C<sub>1</sub>-C<sub>6</sub> alkyl; R<sub>1</sub>/R<sub>2</sub> or R<sub>2</sub>/R<sub>3</sub> together with carbons atoms to which they are attached form a saturated 5-6 membered ring; L = -CH<sub>2</sub>C(O)-, -C(O)CH<sub>2</sub>-, alkyl, alkylene, alkynyl, etc.; G = (un)saturated 5-10 membered ring system which may comprise at least one ring heteroatom selected from nitrogen, oxygen and sulfur, etc.] were prepared as inhibitors of metalloproteinase MMP12 for the treatment of obstructive airways diseases. Thus, reaction of 5-hydantoin acetic acid with ((4'-fluorobiphenyl-4-yl)ethyl)amine yielded compound II. The latter inhibits human MMP12 with an IC<sub>50</sub> = 0.22 μM.

IT 669013-57-4P 669013-58-5P 669013-60-9P  
 669013-61-0P 669013-63-2P 669013-64-3P  
 669013-65-4P 669013-66-5P 669013-67-6P  
 669013-68-7P 669013-69-8P 669013-70-1P  
 669013-72-3P 669013-74-5P 669013-76-7P  
 669013-77-8P 669013-78-9P 669013-79-0P  
 669013-80-3P 669013-82-5P 669013-83-6P  
 669013-84-7P 669013-85-8P 669013-86-9P  
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 669013-90-5P 669013-91-6P 669013-92-7P  
 669013-94-9P 669013-95-0P 669014-00-0P  
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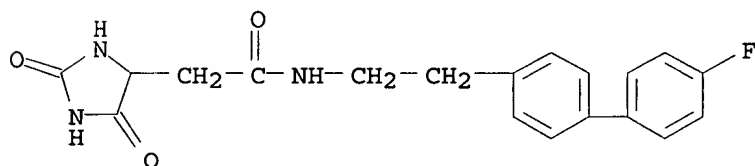
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 669014-92-0P 669014-93-1P 669014-94-2P  
 669014-95-3P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)

(preparation of 2,5-dioxoimidazolidin-4-yl acetamide derivs. as inhibitors  
 of metalloproteinase MMP12)

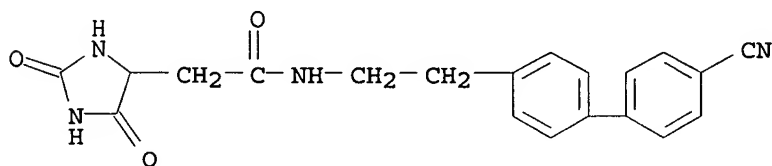
RN 669013-57-4 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-fluoro[1,1'-biphenyl]-4-yl)ethyl]-2,5-  
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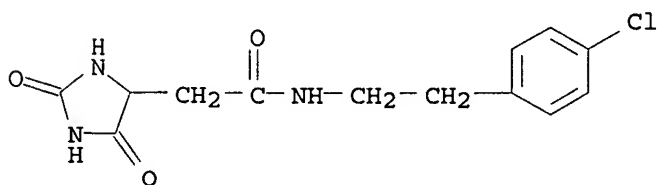
RN 669013-58-5 CAPLUS

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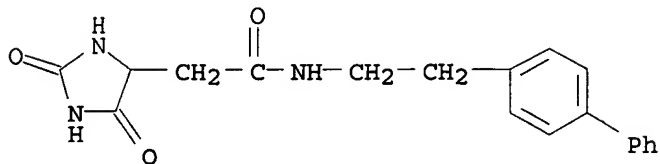
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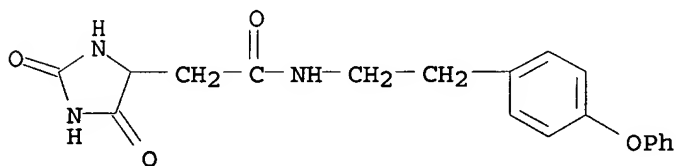
RN 669013-61-0 CAPLUS

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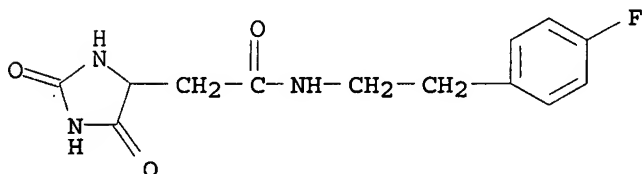
RN 669013-63-2 CAPLUS

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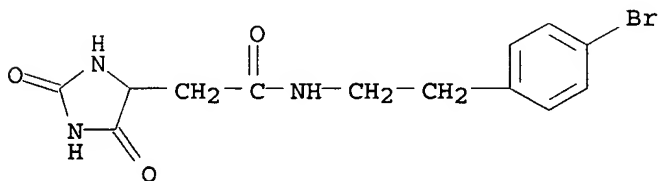
RN 669013-64-3 CAPLUS

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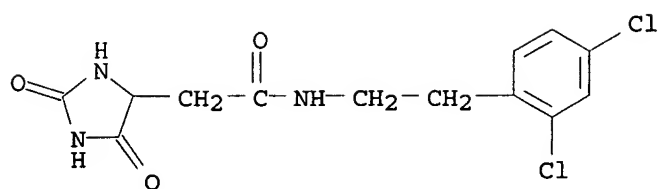
RN 669013-65-4 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4-bromophenyl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



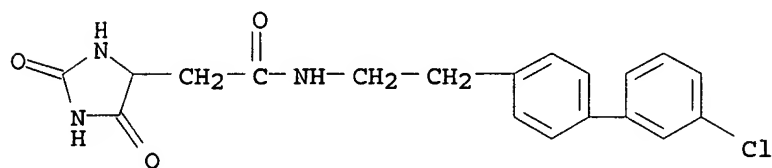
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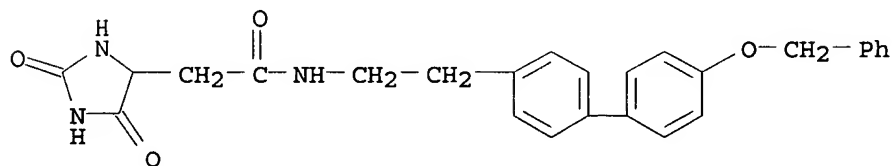
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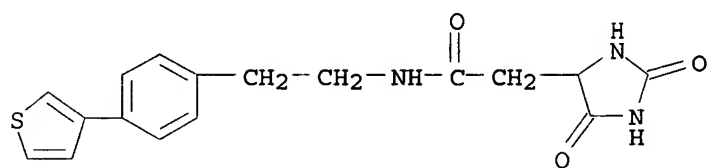
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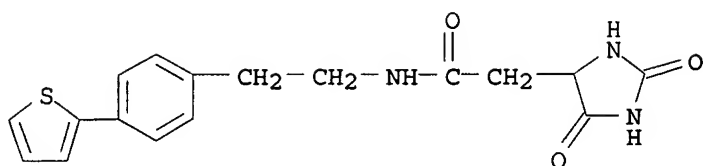
RN 669013-69-8 CAPLUS

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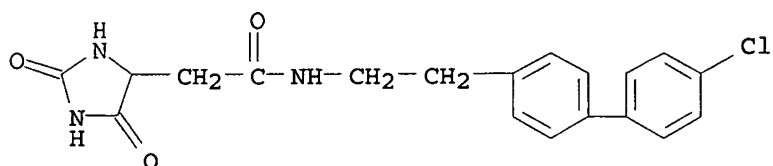
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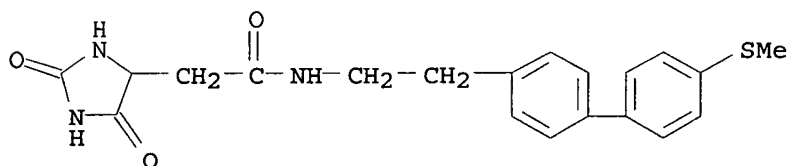
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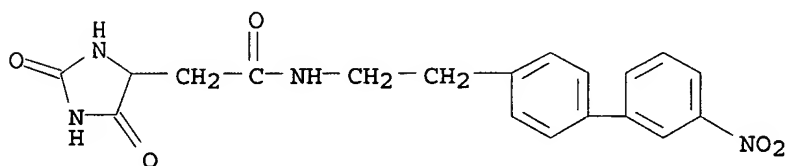
RN 669013-74-5 CAPLUS

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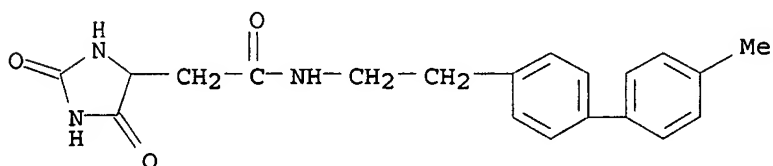
RN 669013-76-7 CAPLUS

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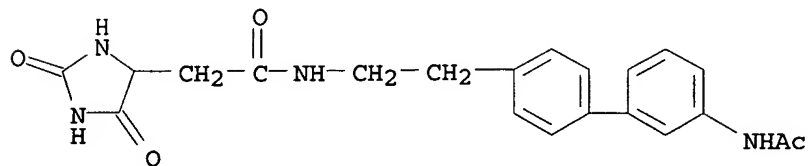
RN 669013-77-8 CAPLUS

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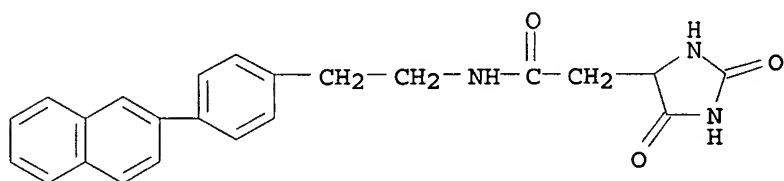
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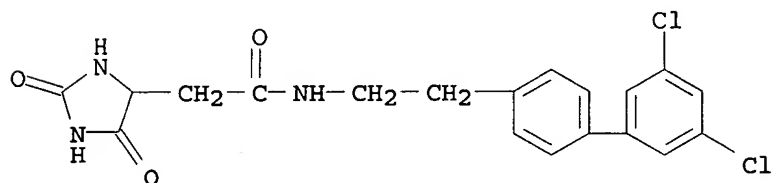
RN 669013-79-0 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(2-naphthalenyl)phenyl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



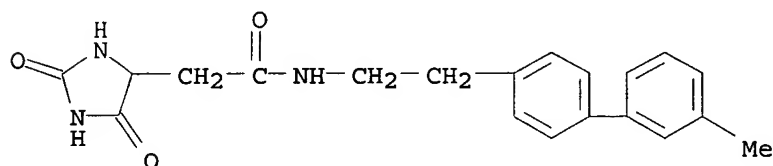
RN 669013-80-3 CAPLUS

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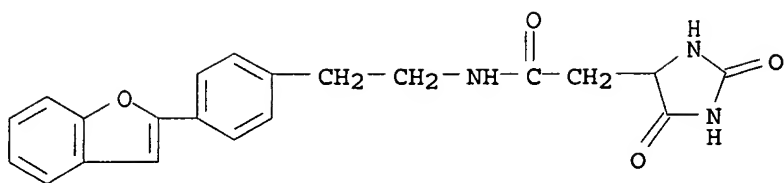
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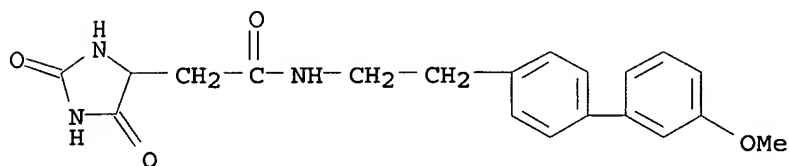
RN 669013-83-6 CAPLUS

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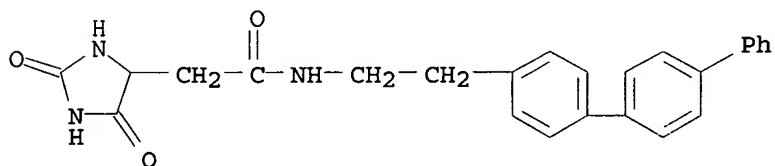
RN 669013-84-7 CAPLUS

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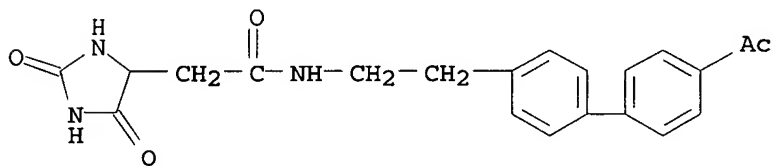
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CN 4-Imidazolidineacetamide, 2,5-dioxo-N-(2-[1,1':4',1''-terphenyl]-4-ylethyl)- (9CI) (CA INDEX NAME)



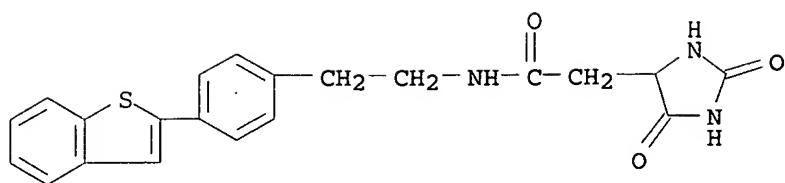
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CN 4-Imidazolidineacetamide, N-[2-(4'-acetyl[1,1'-biphenyl]-4-yl)ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



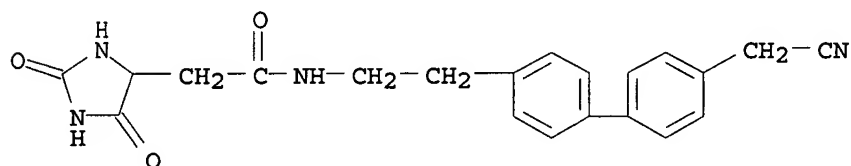
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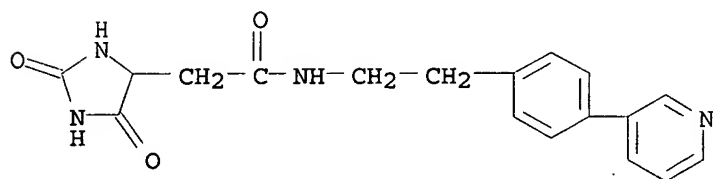
RN 669013-88-1 CAPLUS

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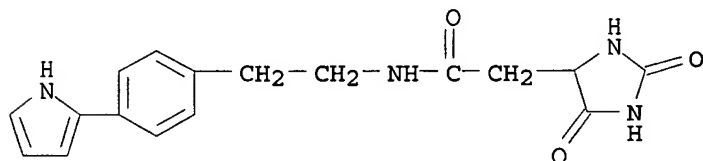
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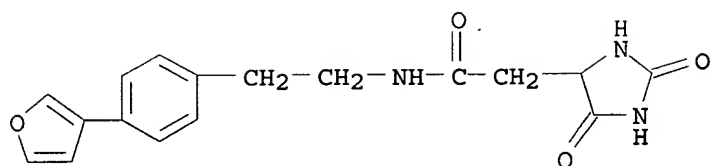
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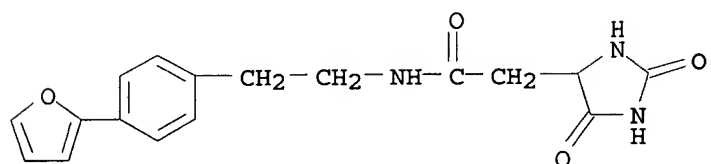


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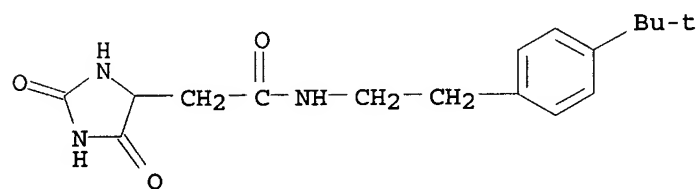
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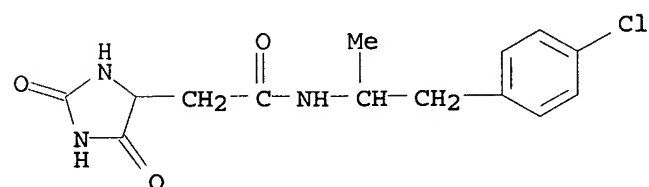
RN 669013-92-7 CAPLUS  
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 (9CI) (CA INDEX NAME)



RN 669013-94-9 CAPLUS  
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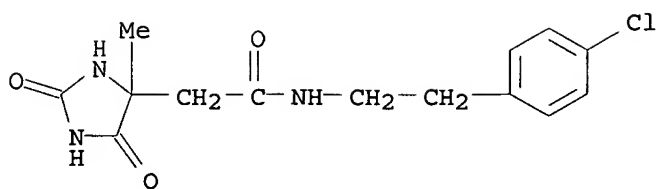


RN 669013-95-0 CAPLUS  
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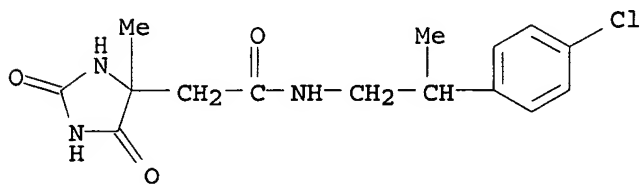
RN 669014-00-0 CAPLUS  
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 (9CI) (CA INDEX NAME)





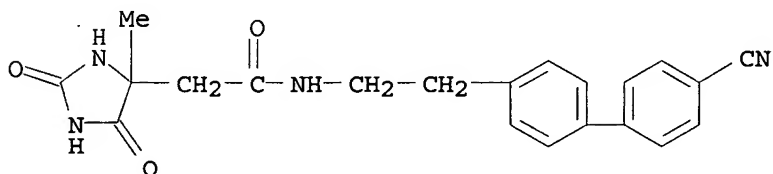
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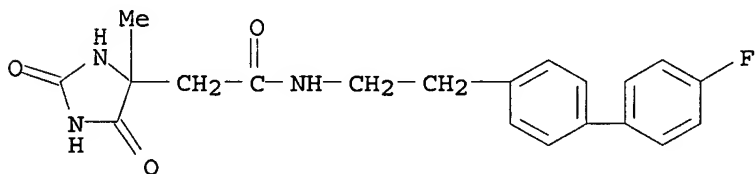
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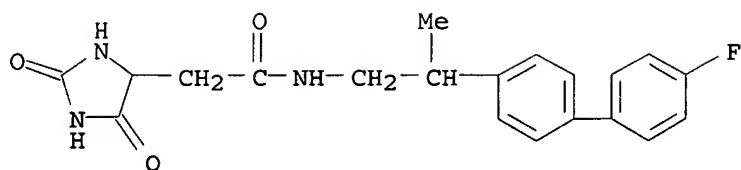
RN 669014-04-4 CAPLUS

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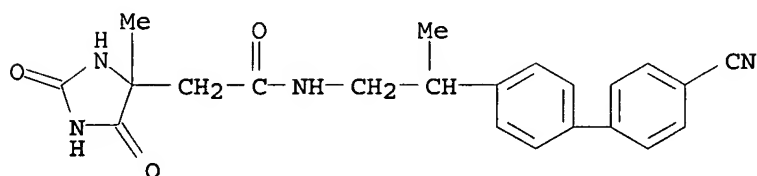
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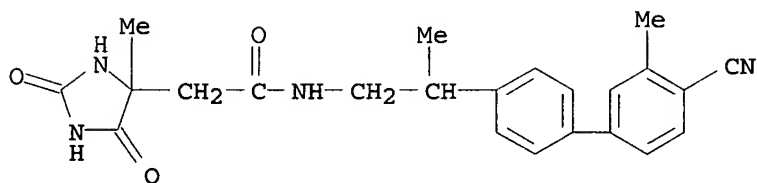
RN 669014-15-7 CAPLUS

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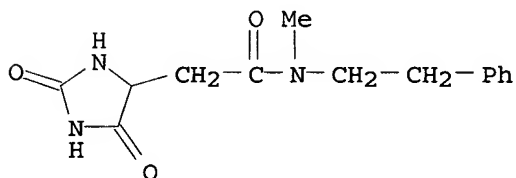
RN 669014-18-0 CAPLUS

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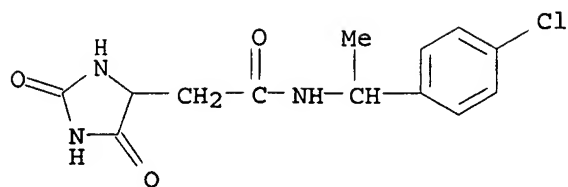
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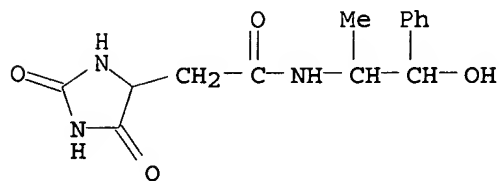
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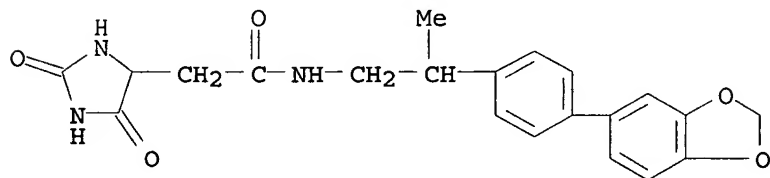
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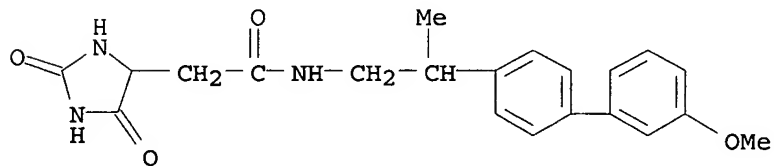
RN 669014-22-6 CAPLUS

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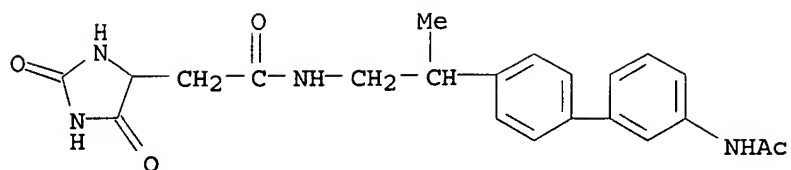
RN 669014-23-7 CAPLUS

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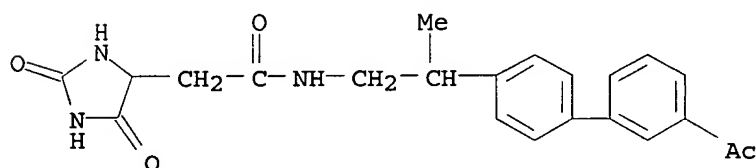
RN 669014-24-8 CAPLUS

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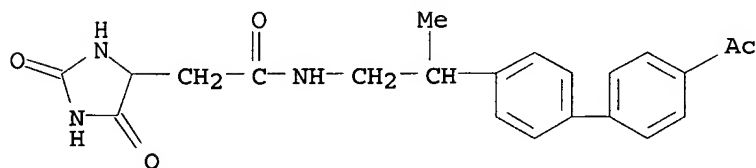
RN 669014-25-9 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3'-acetyl[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



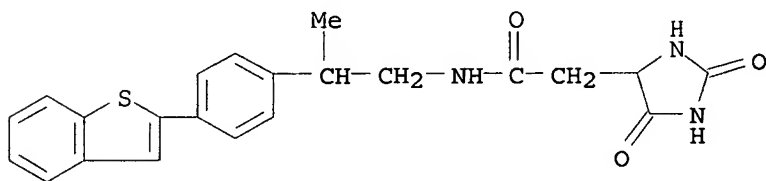
RN 669014-26-0 CAPLUS

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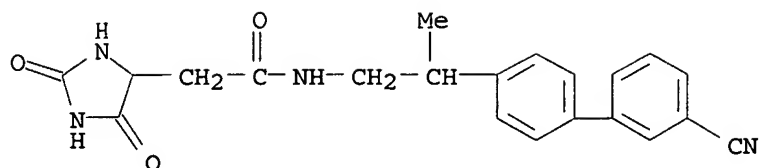
RN 669014-27-1 CAPLUS

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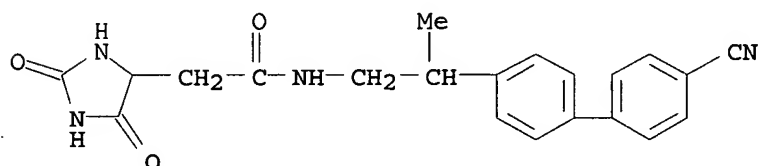
RN 669014-28-2 CAPLUS

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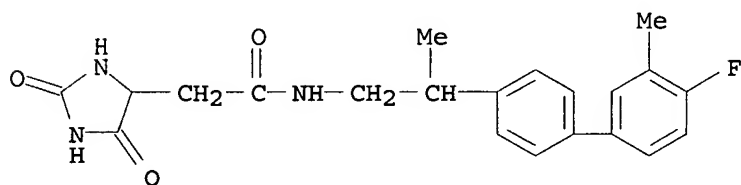
RN 669014-29-3 CAPLUS

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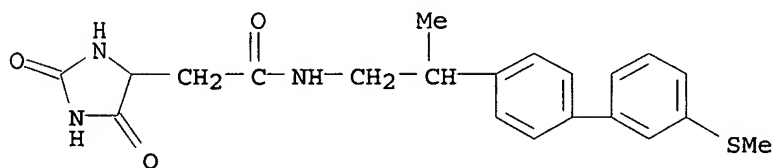
RN 669014-30-6 CAPLUS

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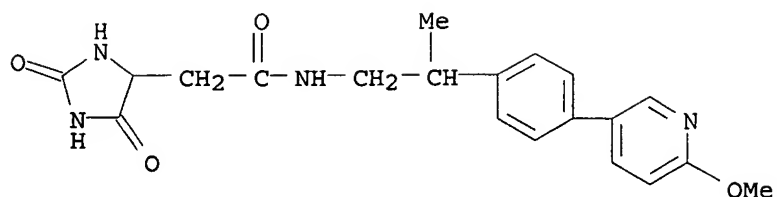
RN 669014-31-7 CAPLUS

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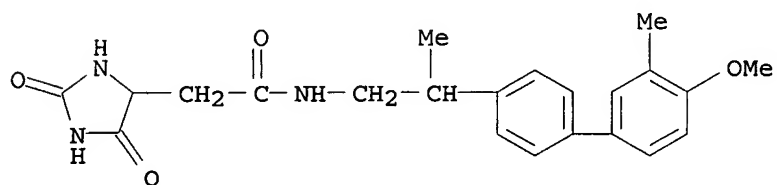
RN 669014-32-8 CAPLUS

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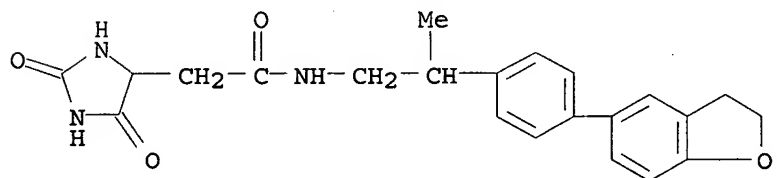
RN 669014-33-9 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-methoxy-3'-methyl[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



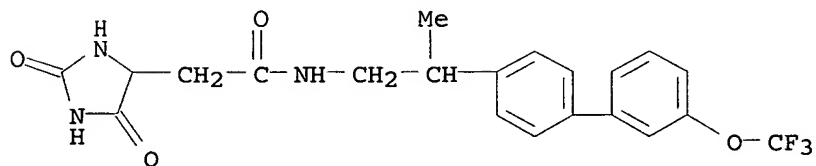
RN 669014-34-0 CAPLUS

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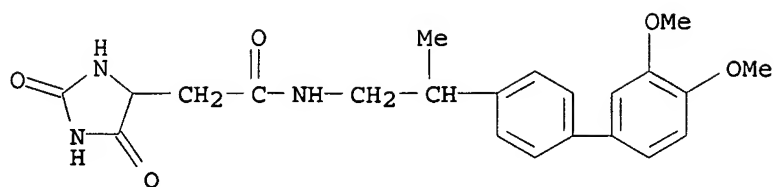
RN 669014-35-1 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]propyl]- (9CI) (CA INDEX NAME)



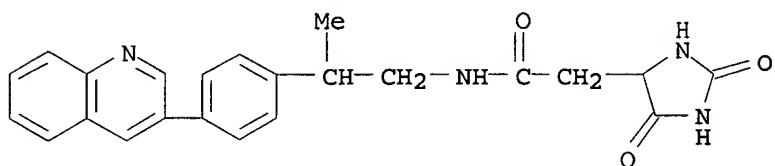
RN 669014-36-2 CAPLUS

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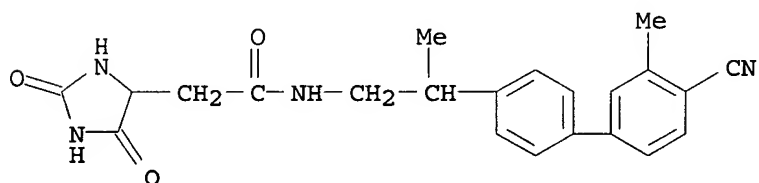
RN 669014-37-3 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4-(3-quinolinyl)phenyl]propyl]- (9CI) (CA INDEX NAME)



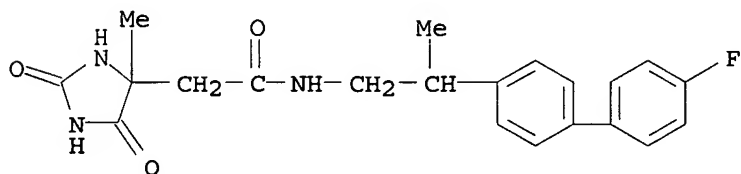
RN 669014-38-4 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-cyano-3'-methyl[1,1'-biphenyl]-4-yl)propyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



RN 669014-53-3 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(4'-fluoro[1,1'-biphenyl]-4-yl)propyl]-4-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)

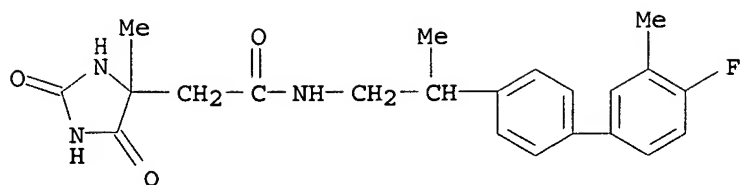


RN 669014-54-4 CAPLUS

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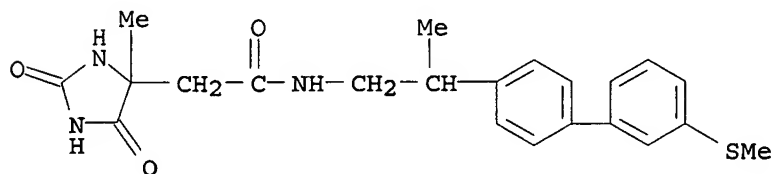






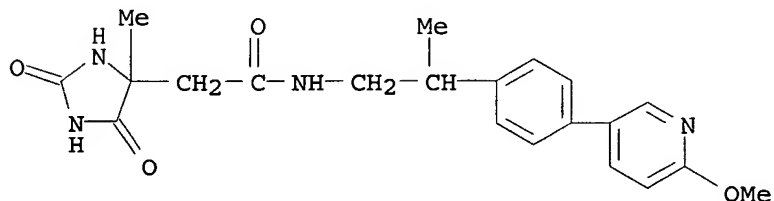
RN 669014-59-9 CAPLUS

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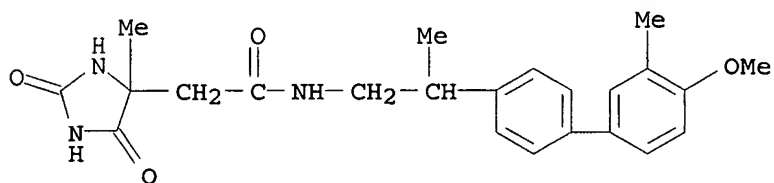
RN 669014-60-2 CAPLUS

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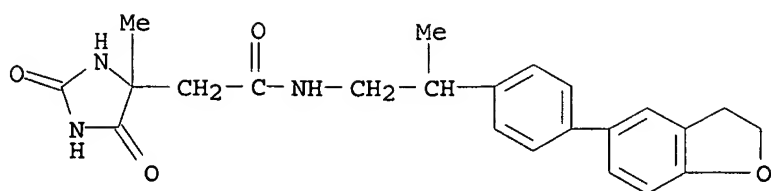
RN 669014-61-3 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-[4-(2,3-dihydro-5-benzofuranyl)phenyl]propyl]-4-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)



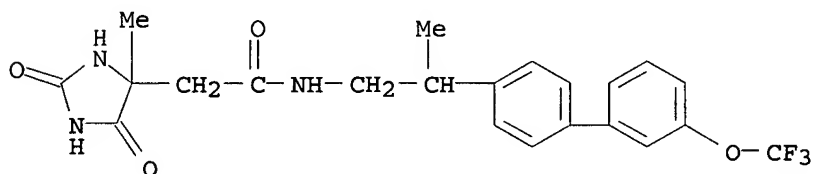
RN 669014-62-4 CAPLUS

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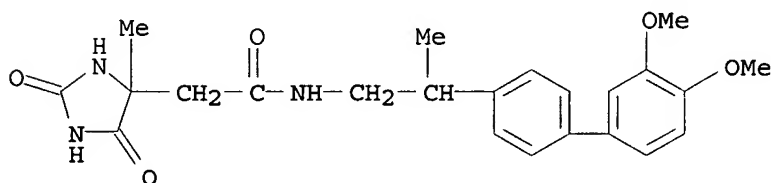
RN 669014-63-5 CAPLUS

CN 4-Imidazolidineacetamide, 4-methyl-2,5-dioxo-N-[2-[3'-(trifluoromethoxy)[1,1'-biphenyl]-4-yl]propyl]- (9CI) (CA INDEX NAME)



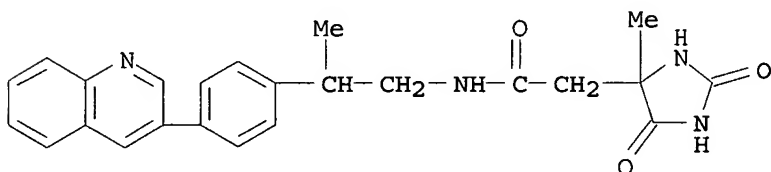
RN 669014-64-6 CAPLUS

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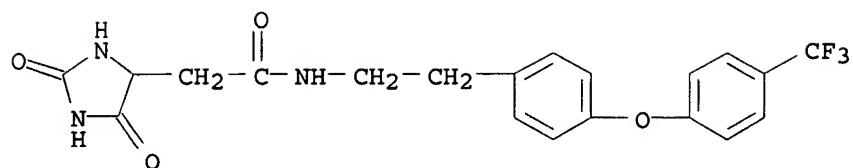
RN 669014-65-7 CAPLUS

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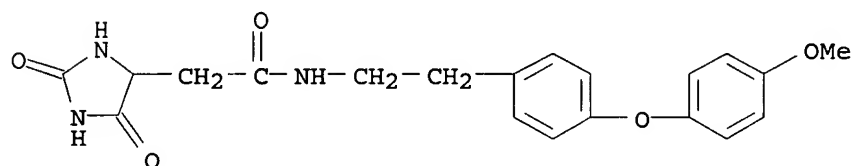
RN 669014-83-9 CAPLUS

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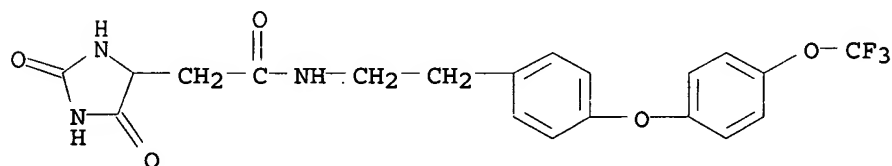
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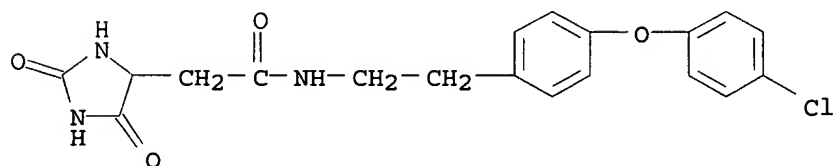
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CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4-[4-(trifluoromethoxy)phenoxy]phenyl]ethyl]- (9CI) (CA INDEX NAME)



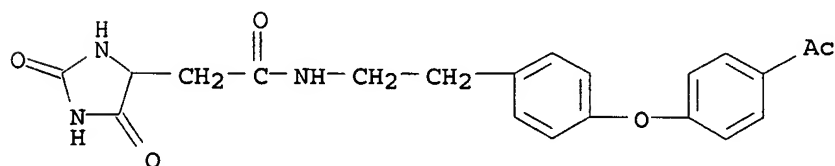
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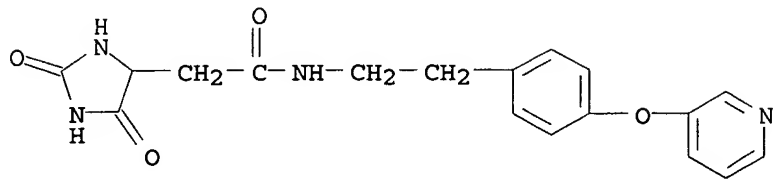
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CN 4-Imidazolidineacetamide, N-[2-[4-(4-acetylphenoxy)phenyl]ethyl]-2,5-dioxo- (9CI) (CA INDEX NAME)



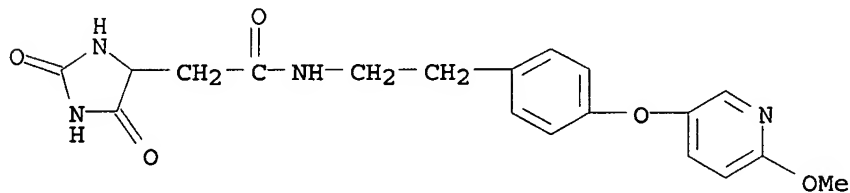
RN 669014-88-4 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-[2-[4-(3-pyridinyloxy)phenyl]ethyl]-  
(9CI) (CA INDEX NAME)



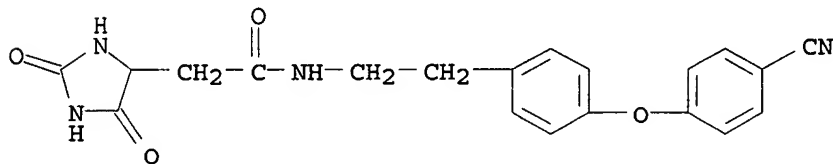
RN 669014-89-5 CAPLUS

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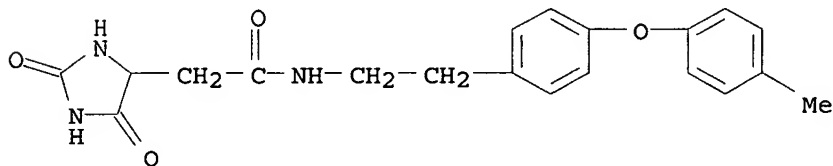
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CN 4-Imidazolidineacetamide, N-[2-[4-(4-cyanophenoxy)phenyl]ethyl]-2,5-dioxo-  
(9CI) (CA INDEX NAME)



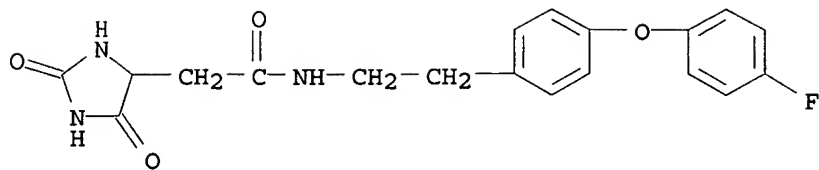
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(9CI) (CA INDEX NAME)



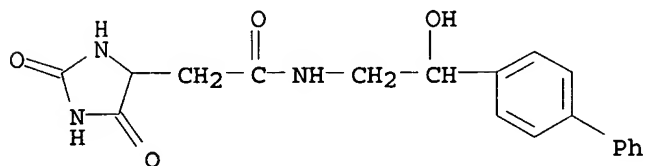
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(9CI) (CA INDEX NAME)



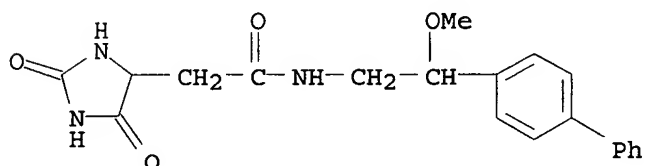
RN 669014-93-1 CAPLUS

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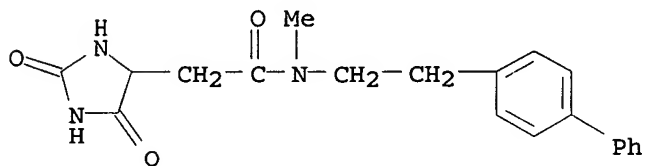
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CN 4-Imidazolidineacetamide, N-(2-[1,1'-biphenyl]-4-yl-2-methoxyethyl)-2,5-dioxo- (9CI) (CA INDEX NAME)



RN 669014-95-3 CAPLUS

CN 4-Imidazolidineacetamide, N-(2-[1,1'-biphenyl]-4-ylethyl)-N-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

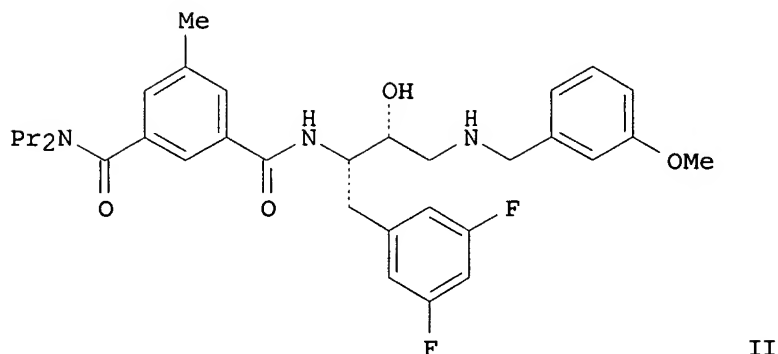
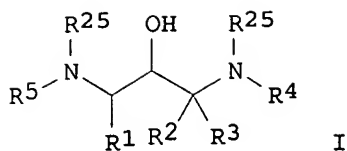
ACCESSION NUMBER: 2003:376819 CAPLUS

DOCUMENT NUMBER: 138:385173

TITLE: Preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease  
INVENTOR(S): Varghese, John; Maillard, Michel; Jagodzinska, Barbara; Beck, James P.; Gailunas, Andrea; Fang, Larry; Sealy, Jennifer; Tenbrink, Ruth; Freskos, John; Mickelson, John; Samala, Lakshman; Hom, Roy  
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn

SOURCE: Company  
PCT Int. Appl., 1243 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003040096	A2	20030515	WO 2002-US36072	20021108
WO 2003040096	A3	20040506		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
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US 2004171881	A1	20040902	US 2002-291318	20021108
EP 1453789	A2	20040908	EP 2002-793909	20021108
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK			
BR 2002014035	A	20050426	BR 2002-14035	20021108
JP 2005520791	T2	20050714	JP 2003-542142	20021108
CN 1759095	A	20060412	CN 2002-826786	20021108
ZA 2004003578	A	20051010	ZA 2004-3578	20040511
NO 2004002359	A	20040806	NO 2004-2359	20040607
PRIORITY APPLN. INFO.:			US 2001-337122P	P 20011108
			US 2001-344086P	P 20011228
			US 2002-345635P	P 20020103
			WO 2002-US36072	W 20021108
OTHER SOURCE(S):	MARPAT 138:385173			
GI				



AB The title compds. [I; R1 = (un)substituted alkyl, alkenyl, alkynyl, etc.; R2 = H, alkyl, haloalkyl, alkenyl, etc.; R3 = H, alkyl, haloalkyl, alkenyl, etc.; or R2 and R3 are taken together with the carbon to which they are attached to form a carbocycle of 3-7 carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of O, S, SO<sub>2</sub>, (un)substituted NH; R4 = alkyl, haloalkyl, hydroxyalkyl, etc.; R5 = R6X (wherein X = CO, SO<sub>2</sub>, (un)substituted CH<sub>2</sub>; R6 = (un)substituted Ph, naphthyl, indanyl, etc.); R25 = H, alkyl, alkoxy, etc.] which have activity as inhibitors of  $\beta$ -secretase and are therefore useful in treating a variety of disorders such as Alzheimer's disease, were prepared E.g., a multi-step synthesis of (1S,2R)-II, starting from (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid, was given. The compds. I showed IC<sub>50</sub> of < 20  $\mu$ M in cell free inhibition assay utilizing a synthetic APP substrate. This is a Part 1 of 1-2 series.

IT 527735-74-6P

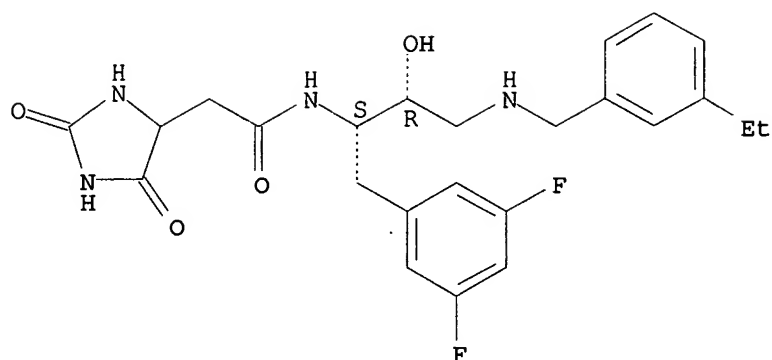
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of N,N'-substituted-1,3-diamino-2-hydroxypropanes for treating Alzheimer's disease)

RN 527735-74-6 CAPLUS

CN 4-Imidazolidineacetamide, N-[(1S,2R)-1-[(3,5-difluorophenyl)methyl]-3-[[[(3-ethylphenyl)methyl]amino]-2-hydroxypropyl]-2,5-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L9 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:927249 CAPLUS

DOCUMENT NUMBER: 138:14059

TITLE: Preparation of spiro-fused hydantoin derivatives as inhibitors of matrix metalloproteinases

INVENTOR(S): Sheppeck, James E.; Duan, Jingwu; Xue, Chu-Biao; Wasserman, Zelda

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 350 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

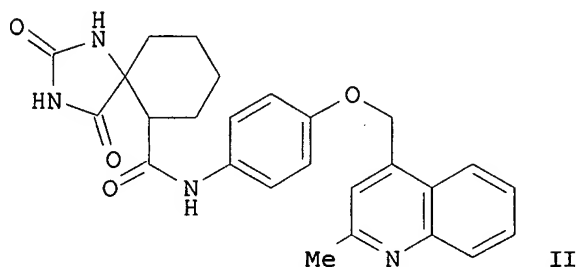
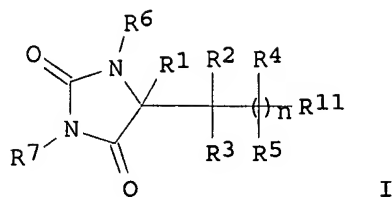
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002096426	A1	20021205	WO 2002-US16381	20020523
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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US 2003130273	A1	20030710	US 2002-155575	20020523
US 6890915	B2	20050510		
EP 1397137	A1	20040317	EP 2002-741724	20020523
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004535411	T2	20041125	JP 2002-592936	20020523
US 2004209874	A1	20041021	US 2004-844219	20040512
US 6906053	B2	20050614		
US 2005171096	A1	20050804	US 2005-93670	20050330
PRIORITY APPLN. INFO.:				
			US 2001-293571P	P 20010525
			US 2002-155575	A3 20020523
			WO 2002-US16381	W 20020523
			US 2004-844219	A3 20040512

OTHER SOURCE(S): MARPAT 138:14059

GI





AB Title compds. I [R11 = W-U-X-Y-Z-Ua-Xa-Ya-Za; W = alkyl, alkenylene, alkynylene; U = absent, amino, CO, alkyl, carboxy, etc.; X = absent, alk(en/yn)ylene; Y = absent, O, amino, SOO-2, CO; Z = (hetero)cycle; Ua = absent, O, amino, CO, alkyl, carboxy, etc.; Xa = absent, alk(en/yn)ylene; Ya = absent, O, amino, SOO-2, CO; Za = (hetero)cycle; R1-2 together with the carbon atoms to which they are attached, combine to form a 3-8 membered carbocyclic or heterocyclic ring; R3 = H, CHF2, CH2F, CF3, alk(en/yn)ylene, etc.; R4-7 = H, alk(en/yn)yl; n = 0-1] were prepared. For instance, 2-(ethylcarboxy)cyclohexanone was treated with ammonium carbonate and potassium cyanide (EtOHaq, 50°, 24 h) to afford the corresponding hydantoin ester which was hydrolyzed to the carboxylic acid and coupled to 4-[(2-methyl-4-quinolinyl)methoxy]aniline•2HCl (DMSO, PyBOP) to give II which was isolated as the trifluoroacetate. I are useful as inhibitors of matrix metalloproteinases (MMP), TNF- $\alpha$  converting enzyme (TACE), aggrecanase, or a combination thereof.

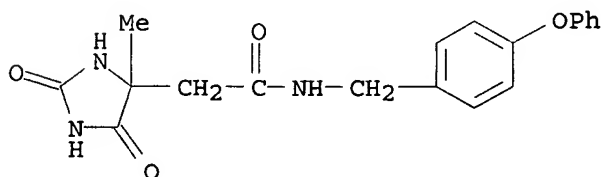
IT 477583-00-9P, 2-(4-Methyl-2,5-dioxo-4-imidazolidinyl)-N-(4-phenoxybenzyl)acetamide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(hydantoin derivs. as inhibitors of matrix metalloproteinases)

RN 477583-00-9 CAPLUS

CN 4-Imidazolidineacetamide, 4-methyl-2,5-dioxo-N-[(4-phenoxyphenyl)methyl]-(9CI) (CA INDEX NAME)



REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:640897 CAPLUS

DOCUMENT NUMBER: 137:337840

TITLE: Use of Statistical Design of Experiments in the  
Optimization of Amide Synthesis Utilizing  
Polystyrene-Supported N-Hydroxybenzotriazole Resin

AUTHOR(S): Gooding, Owen W.; Vo, Lanchi; Bhattacharyya, Sukanta;  
Labadie, Jeff W.

CORPORATE SOURCE: Argonaut Technologies, Foster City, CA, 94404, USA

SOURCE: Journal of Combinatorial Chemistry (2002), 4(6),  
576-583

CODEN: JCCHFF; ISSN: 1520-4766

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:337840

AB Statistical process optimization is used to determine appropriate reagents, order of addition, and stoichiometry for amidation reactions of amines and carboxylic acids using a resin-bound hydroxybenzotriazole coupling reagent. Previous reactions used the expensive coupling reagent PyBOP and carboxylic acids in excess and required the premixing of reagents, both of which are not amenable either to automated synthesis or to the preparation of combinatorial libraries. The less expensive coupling reagent diisopropyl carbodiimide (DIC) is used instead of PyBOP with 4-(dimethylamino)pyridine as a catalyst. Using these reagents, it is important that the acid be added first; neither the time of addition nor the amount of acid is important if sufficient DIC (optimally 4.4 equivalent) is used. A mixture of DMF and methylene chloride is the optimal solvent; the fraction of DMF is minimized to maximize the amount of acid coupled to the resin-bound hydroxybenzotriazole. The type of acid also affects the efficiency of coupling. This routine is used to generate a combinatorial library of amides by coupling of amines and carboxylic acids; the products are isolated by filtration of the hydroxybenzotriazole resin followed by removal of solvent.

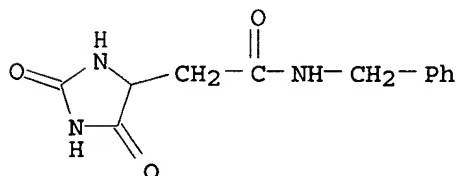
IT 473254-15-8P

RL: CPN (Combinatorial preparation); CMBI (Combinatorial study); PREP (Preparation)

(statistical process optimization for amidation reactions using a resin-bound hydroxybenzotriazole and their use in the preparation of a combinatorial library of amides from amines and carboxylic acids)

RN 473254-15-8 CAPLUS

CN 4-Imidazolidineacetamide, 2,5-dioxo-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

14

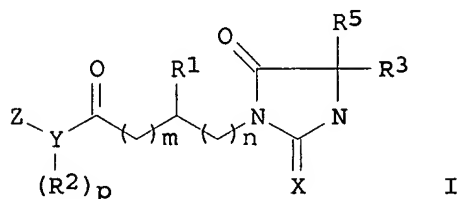
THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

10525640.trn

ACCESSION NUMBER: 1998:543055 CAPLUS  
 DOCUMENT NUMBER: 129:161842  
 TITLE: Preparation and biological testing of  
 dipeptide-derived hydantoin and thiohydantoin  
 combinatorial libraries  
 INVENTOR(S): Meyer, Jean-Philippe; Ostresh, John M.; Houghten,  
 Richard A.  
 PATENT ASSIGNEE(S): Trega Biosciences, Inc., USA  
 SOURCE: PCT Int. Appl., 122 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9833776	A1	19980806	WO 1997-US22388	19971205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5859190	A	19990112	US 1997-794363	19970204
AU 9853761	A1	19980825	AU 1998-53761	19971205
PRIORITY APPLN. INFO.:			US 1997-794363	A 19970204
			WO 1997-US22388	W 19971205
OTHER SOURCE(S):			MARPAT 129:161842	
GI				



AB The invention provides a rapid approach for combinatorial synthesis and screening of dipeptide-derived hydantoin and thiohydantoin compds. and combinatorial libraries and sublibraries I [R1, R3 independently = H, (un)substituted C1-10 alkyl, (un)substituted C7-16 phenylalkyl, (un)substituted Ph, (un)substituted amino, (un)substituted carboxy, (un)substituted carbamoyl, (un)substituted C3-7 cycloalkyl; R2, R4, R5 independently = H, C1-10 alkyl, C2-10 alkenyl, (un)substituted benzyl, (un)substituted naphthylmethyl; X = O, S; Y = N, p = 1, Z = H, amino resin; Y = O, p = 0, Z = H, hydroxy resin; m = 0-5; n = 0-4]. Relative reaction rates for solid-phase peptide coupling of 139 N-protected amino acid derivs. are also given. Thus, nearly 600 hydantoin and thiohydantoin combinatorial libraries and sublibraries I were prepared and tested for antibacterial activity and opioid receptor binding selectivity.

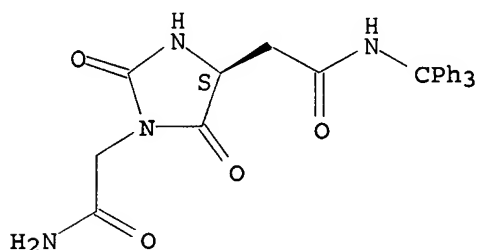
IT 211253-17-7DP, combinatorial libraries containing  
 211253-18-8DP, combinatorial libraries containing  
 211253-19-9DP, combinatorial libraries containing

211253-67-7DP, combinatorial libraries containing  
 211253-68-8DP, combinatorial libraries containing  
 211253-69-9DP, combinatorial libraries containing  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation and biol. testing of dipeptide-derived hydantoin and thiohydantoin combinatorial libraries)

RN 211253-17-7 CAPLUS

CN 1,4-Imidazolidinediacetamide, 2,5-dioxo-N4-(triphenylmethyl)-, (4S)- (9CI)  
 (CA INDEX NAME)

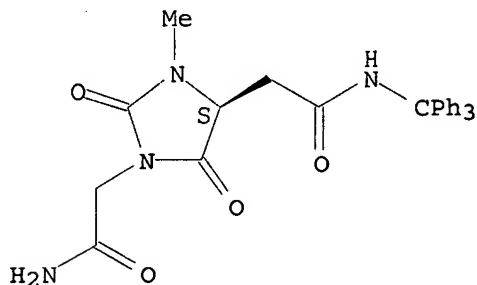
Absolute stereochemistry.



RN 211253-18-8 CAPLUS

CN 1,4-Imidazolidinediacetamide, 3-methyl-2,5-dioxo-N4-(triphenylmethyl)-, (4S)- (9CI) (CA INDEX NAME)

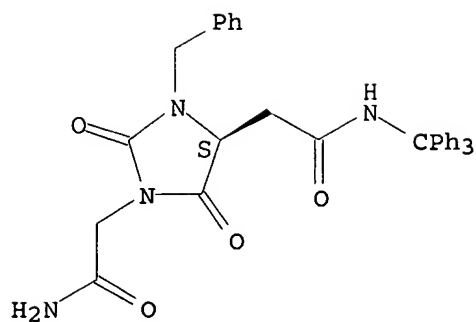
Absolute stereochemistry.



RN 211253-19-9 CAPLUS

CN 1,4-Imidazolidinediacetamide, 2,5-dioxo-3-(phenylmethyl)-N4-(triphenylmethyl)-, (4S)- (9CI) (CA INDEX NAME)

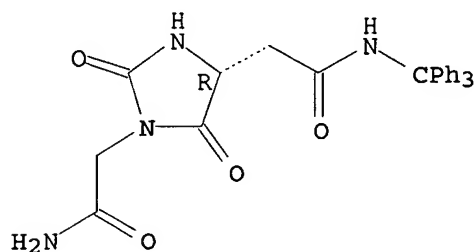
Absolute stereochemistry.



RN 211253-67-7 CAPLUS

CN 1,4-Imidazolidinediacetamide, 2,5-dioxo-N4-(triphenylmethyl)-, (4R)- (9CI)  
(CA INDEX NAME)

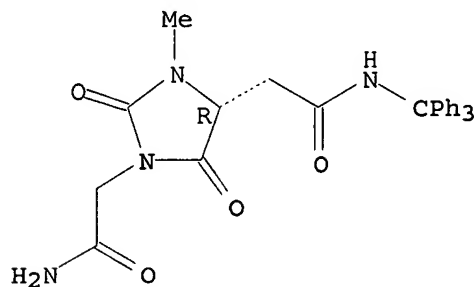
Absolute stereochemistry.



RN 211253-68-8 CAPLUS

CN 1,4-Imidazolidinediacetamide, 3-methyl-2,5-dioxo-N4-(triphenylmethyl)-, (4R)- (9CI) (CA INDEX NAME)

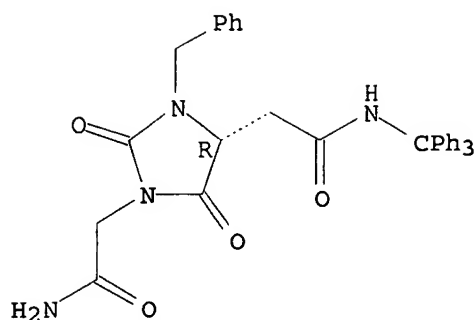
Absolute stereochemistry.



RN 211253-69-9 CAPLUS

CN 1,4-Imidazolidinediacetamide, 2,5-dioxo-3-(phenylmethyl)-N4-(triphenylmethyl)-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:388199 CAPLUS

DOCUMENT NUMBER: 125:58489

TITLE: Preparation of N-acylated 2-heterocycloethylamines as nonpeptide antagonists of SP and NKA

INVENTOR(S): Russell, Keith

PATENT ASSIGNEE(S): Zeneca Limited, UK; Astrazeneca AB

SOURCE: Eur. Pat. Appl., 40 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 709375	A2	19960501	EP 1995-307496	19951020
EP 709375	A3	19980826		
EP 709375	B1	20050518		
R: CH, DE, ES, FR, GB, IT, LI				
JP 08208605	A2	19960813	JP 1995-275847	19951024
US 5710169	A	19980120	US 1995-547512	19951024
US 5998444	A	19991207	US 1997-979995	19971126
US 6147083	A	20001114	US 1999-384444	19990827
PRIORITY APPLN. INFO.:			GB 1994-21411	A 19941025
			GB 1995-12367	A 19950617
			US 1995-547512	A3 19951024
			US 1997-979995	A3 19971126

OTHER SOURCE(S): CASREACT 125:58489; MARPAT 125:58489  
GI



AB The title compds. [I; Q1 = (substituted) piperidino, piperazino, pyrrolidino, etc.; Q2, Q3 = H, C1-3 alkyl; Q4 = (substituted) Ph, thienyl, imidazolyl, etc.; Q5 = (substituted) C1-8 alkyl, aryl, formyl, etc.] and

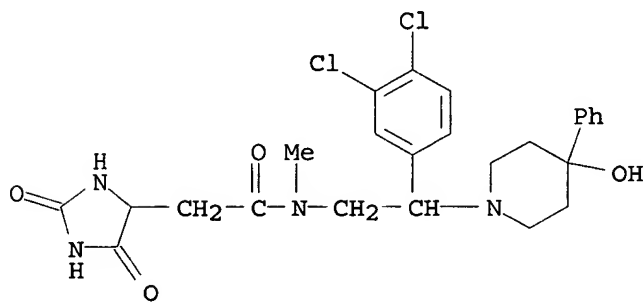
its salts, useful for the treatment of asthma, were prepared by acylation of amine II with the corresponding acid or acid chloride. Thus, acylation of the piperidinoethylamine II [Q1 = 4-hydroxy-4-phenylpiperidino; Q2 = Me; Q3 = H; Q4 = 3,4-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>] with 2-MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>COOH in the presence of 1,1'-carbonyldiimidazole in THF followed by treatment with HCl afforded I.HCl [Q5 = 2-MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>]. In general, compds. I showed K<sub>i</sub> of ≤ 1 μM against SP receptor binding and K<sub>i</sub> ≤ 10 μM against neurokinin A (NKA) receptor binding.

IT 178166-64-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of N-acylated 2-heterocycloethylamines as nonpeptide antagonists of SP and NKA)

RN 178166-64-8 CAPLUS

CN 4-Imidazolidineacetamide, N-[2-(3,4-dichlorophenyl)-2-(4-hydroxy-4-phenyl-1-piperidiny)ethyl]-N-methyl-2,5-dioxo- (9CI) (CA INDEX NAME)



L9 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1949:6377 CAPLUS

DOCUMENT NUMBER: 43:6377

ORIGINAL REFERENCE NO.: 43:1352c-i,1353a-b

TITLE: Diethyl N-benzyl-DL-aspartate and related compounds

AUTHOR(S): McMillan, Freeman H.; Albertson, Noel F.

SOURCE: Journal of the American Chemical Society (1948), 70, 3778-81

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB (:CHCO)2O (49 g.), 107 g. PhCH<sub>2</sub>NH<sub>2</sub>, and 200 ml. H<sub>2</sub>O, refluxed 25 hrs., 119 g. 35% NaOH added, the mixture refluxed an addnl. 24 hrs., poured into ice and excess HCl, the residue refluxed 4 hrs. with 1000 ml. 2% EtOH-HCl, and the product covered with 600 ml. C<sub>6</sub>H<sub>6</sub> and treated with excess NaOH, give 20% di-Et N-benzyl-DL-aspartate (I), b<sub>0.5</sub> 136°, n<sub>25D</sub> 1.4931. Crude EtO<sub>2</sub>CCH<sub>2</sub>CHClCO<sub>2</sub>Et (41.7 g.), 42.8 g. PhCH<sub>2</sub>NH<sub>2</sub>, and 200 ml. C<sub>6</sub>H<sub>6</sub>, refluxed 1 hr., give 47% I. Hydrolysis of 5 ml. I with 100 ml. concentrated HCl (refluxed 5 hrs.) gives N-benzyl-DL-aspartic acid, m. 194-7° (decomposition). EtO<sub>2</sub>CCOCH<sub>2</sub>CO<sub>2</sub>Et (18.8 g.) and 10.7 g. PhCH<sub>2</sub>NH<sub>2</sub> in 125 ml. AcOEt, shaken with H and Pt oxide, give presumably N,N'-dibenzylmalamide, m. 144-5°. (:CHCO)2O (1 mole) and 2 moles H<sub>2</sub>NCH<sub>2</sub>CO<sub>2</sub>H in 400 ml. H<sub>2</sub>O, refluxed 20 hrs., the solution treated with 4.6 moles 40% NaOH and 200 ml. H<sub>2</sub>O, the mixture refluxed an addnl. 20 hrs., the product poured into 700 ml. concentrated HCl and concentrated to dryness, and the residue in 1 l.

EtOH saturated

with HCl and refluxed 3 hrs., give 20% di-Et N-(carbethoxymethyl)-DL-

aspartate, b0.3 130-40°, n<sub>25D</sub> 1.4429; refluxed 8 hrs. with BzCl in C<sub>6</sub>H<sub>6</sub> it yields the Bz derivative, very viscous oil, b. 170°/5 + 10-4 mm. (bath temperature). Di-Et fumarate (II) (17.2 g.) and 21.9 g. PhCH<sub>2</sub>NH<sub>2</sub>, heated 45 min. at 250°, give 3 g. N, 'N', 'N', 'N'-tetrabenzoyldiketopiperazinediacetamide(?) (III), m. 294-6°; if the reactants are heated 4 hrs. at 150-60° and the product extracted with 600 ml. ether, there results a residue of 18 g. of N $\alpha$ ,N,N'-tribenzyl-DL-aspartamide (IV), m. 146-8°; the ether yields 28 g. N-benzyl- $\alpha$ -benzylaminosuccinimide (V), m. 61.2-2.5°, and 25 g. of an oil (VI). IV, heated 10 min. at 250°, yields III. V yields a HCl salt, m. 193-5°, and a NO derivative, m. 129.5-30.5°. V (1.94 g.) and 30 ml. 10% EtOH-KOH, refluxed 4 hrs., give 81%  $\alpha$ -benzylamino-N-benzylsuccinamic acid (VII), m. 215° (decomposition); IV yields 50% VII and VI yields 1/3 its weight of VII. II (43 g.) and 80.5 g. PhCH<sub>2</sub>NH<sub>2</sub>, heated 4 hrs. at 150-60°, and the crude product refluxed 2 hrs. with 1 l. 10% EtOH-KOH, give 57% VII; with 2 mols. PhCH<sub>2</sub>NH<sub>2</sub> the yield is 45%. VII (6.24 g.) in 100 ml. AcOH, shaken with H at 60° in the presence of 0.3 g. C containing 10% PdCl<sub>2</sub>, gives 90%  $\alpha$ -amino-N-benzylsuccinamic acid (VIII), m. 265° (decomposition). VII (15.6 g.) in 100 ml. EtOH, treated with HCl until the solution is saturated at its b.p. and refluxed 0.5 hr., gives 90% Et  $\alpha$ -benzylamino-N-benzylsuccinamate-HCl, m. 154° (decomposition). VII (3 g.) in 25 ml. H<sub>2</sub>O and 5 ml. HCl, treated dropwise with 0.8 g. NaNO<sub>2</sub> in 5 ml. H<sub>2</sub>O, gives N-benzyl- $\alpha$ -hydroxysuccinamic acid, m. 113°. V (3.2 g.) in 100 ml. AcOH, reduced at 50° with H and 5% Pd-C and the residue refluxed 20 min. with Ac<sub>2</sub>O, gives 1.3 g.  $\alpha$ -acetamido-N-benzylsuccinimide (IX), m. 174-5.6° (corrected); IX results also on shaking VIII and Ac<sub>2</sub>O in AcOH (6 hrs.). Addition of 36 g. AcNHCH(CO<sub>2</sub>Et)<sub>2</sub>, 31.5 g. ClCH<sub>2</sub>CONH-CH<sub>2</sub>Ph, and 0.5 g. NaI to 3.8 g. Na in 300 ml. EtOH and keeping the solution 48 hrs. at room temperature give 22 g. IX; there results

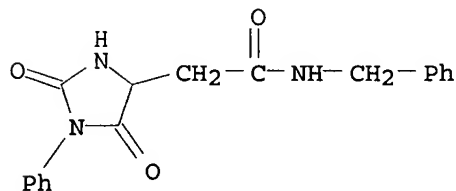
also

16.9 g.  $\alpha$ -acetamido-N-benzyl- $\alpha$ -carbethoxysuccinimide (X), m. 125-6°. IX or X, refluxed 3 hrs. with 10% Na<sub>2</sub>CO<sub>3</sub>, gives  $\alpha$ -acetamido-N-benzylsuccinamic acid, m. 153-5°; heated above its m.p., it yields IX; VII results on refluxing 2 hrs. with 10% EtOH-KOH. VIII (4 g.), 3 g. NH<sub>4</sub>SCN, 18 ml. Ac<sub>2</sub>O, and 2 ml. AcOH, warmed 1.5 hrs. on the steam bath, give 4.1 g. 1-acetyl-N-benzyl-2-thio-5-hydantoinacetamide, m. 162-4°; VIII and PhSCN give  $\alpha$ -(3-phenylureido)-N-benzylsuccinamic acid, m. 180-1.5°; refluxed 45 min. with 12% HCl it yields N-benzyl-3-phenyl-5-hydantoinacetamide, m. 166-7° (decomposition); refluxed 2 hrs. with HCl, this gives 3-phenyl-5-hydantoinacetic acid. DL-Aspartic acid results in 53% yield from ClCH<sub>2</sub>CO<sub>2</sub>Et and AcNHCH(CO<sub>2</sub>Et)<sub>2</sub>, followed by hydrolysis.

IT 858208-03-4, 5-Hydantoinacetamide, N-benzyl-3-phenyl-  
(preparation of)

RN 858208-03-4 CAPLUS

CN 5-Hydantoinacetamide, N-benzyl-3-phenyl- (5CI) (CA INDEX NAME)





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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

48.80

389.59

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-6.75

-6.75

STN INTERNATIONAL LOGOFF AT 18:03:57 ON 18 APR 2006